Clinical trial results:
An Open Label, Dose Escalation, Multicenter Phase 1/2 Study of KW-2478 in Combination with Bortezomib in Subjects with Relapsed and/or Refractory Multiple Myeloma

Summary

EudraCT number	2009-016223-56
Trial protocol	GB
Global end of trial date	19 September 2013

Results information

Result version number	v1 (current)
This version publication date	27 July 2016
First version publication date	27 July 2016

Trial information

Trial identification

Sponsor protocol code	2478-INT-001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Kyowa Hakko Kirin Pharma, Inc.
Sponsor organisation address	212 Carnegie Centre, Suite 101, Princeton, United States, NJ 08540
Public contact	Kurman, Kyowa Hakko Kirin Pharma, Inc., clinical.info@kyowa-kirin-pharma.com
Scientific contact	Kurman, Kyowa Hakko Kirin Pharma, Inc., clinical.info@kyowa-kirin-pharma.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	26 March 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 September 2013
Global end of trial reached?	Yes
Global end of trial date	19 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to assess the safety and benefits of the investigational study drug, KW-2478, when given with bortezomib (Velcade®), a drug approved for the treatment of Multiple Myeloma (MM).

The primary objectives:
- To establish the safety, tolerability, and recommended Phase II dose (RP2D) of KW-2478 in combination with bortezomib (Phase I);

- To assess the overall response rate (ORR) when subjects with advanced MM are treated (Phase II).

The secondary objectives:
- To characterize the Pharmacokinetic (PK) and Pharmacodynamic (PD) of KW-2478 with bortezomib (Phase I only);
- To evaluate for preliminary evidence of efficacy (Phase I);
- To determine progression free survival (PFS) and duration of response of KW-2478 with bortezomib (Phase II).

Protection of trial subjects:

ICF includes all details

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 57
Country: Number of subjects enrolled	United States: 18
Country: Number of subjects enrolled	Philippines: 20
Worldwide total number of subjects	95
EEA total number of subjects	57

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)	47
From 65 to 84 years	48
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study centers in the USA and the UK participated in the Phase 1 portion, and study centers in the USA, UK, and Philippines participated in the Phase 2 portion.

Pre-assignment

Screening details:

Inclusion / Exclusion criteria

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Phase 1: KW-2478 and Bortezomib

Arm description:

The target population in Phase 1 were adults (≥18 years) of either gender with a confirmed history of MM by IMWG criteria had relapsed or failed to respond to 1–3 prior MM regimens with an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 and a life expectancy ≥ 3 months. Subjects had to have disease that could be evaluated by serum or urinary levels of M protein or serum free light chains in the absence of measurable M protein in serum or urine.

For Phase 1, the design was a standard 3+3 study of KW-2478 (130 or 175 mg/m^2) and bortezomib(1.0 or 1.3 mg/m^2) on Days 1, 4, 8, and 11 of a 21-day cycle utilizing four dose-escalation

Arm type	Experimental
Investigational medicinal product name	KW-2478
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

130mg/m2

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.0mg/m2

Arm title	Phase II: KW-2478 130mg/m^2 and Bortezomib 1.3mg/m^2

Arm description:

The target population in Phase 2 were adults (≥18 years) of either gender with a confirmed history of MM by IMWG criteria had relapsed or failed to respond to 1–3 prior MM regimens with an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 and a life expectancy ≥ 3 months. Subjects had to have disease that could be evaluated by serum or urinary levels of M protein or serum free light chains in the absence of measurable M protein in serum or urine.
For the Phase 2 portion of the study was designed to determine the preliminary efficacy of KW 2478 and bortezomib at the RP2D (KW-2478 175 mg/m^2/bortezomib1.3 mg/m^2).

Arm type	Experimental

Investigational medicinal product name	KW-2478
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

175mg/m2

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.3mg/m2

Arm title	KW-2478 and bortezomib

Arm description:

The target population in both Phase 1 and 2 were adults (≥18 years) of either gender with a confirmed history of MM by IMWG criteria had relapsed or failed to respond to 1–3 prior MM regimens with an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 and a life expectancy ≥ 3 months. Subjects had to have disease that could be evaluated by serum or urinary levels of M protein or serum free light chains in the absence of measurable M protein in serum or urine.
For Phase 1, the design was a standard 3+3 study of KW-2478 (130 or 175 mg/m^2) and Bortezomib(1.0 or 1.3 mg/m^2) on Days 1, 4, 8, and 11 of a 21-day cycle utilizing four dose-escalation cohorts (overall N=15). The Phase 2 portion of the study enrolled 80 subjects to determine the preliminary efficacy of KW 2478 and Bortezomib at the RP2D (KW-2478 175 mg/m^2 / Bortezomib 1.3

Arm type	Experimental
Investigational medicinal product name	KW-2478
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

175mg/m2

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.3mg/m2

Arm title	Phase 1 & 2: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2

Arm description:

The target population in both Phase 1 and 2 were adults (≥18 years) of either gender with a confirmed history of MM by IMWG criteria had relapsed or failed to respond to 1–3 prior MM regimens with an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 and a life expectancy ≥ 3 months. Subjects had to have disease that could be evaluated by serum or urinary levels of M protein or serum free light chains in the absence of measurable M protein in serum or urine.

The Phase 1 portion of the study was a standard 3+3 study design of KW-2478 (130 or 175 mg/m^2) and Bortezomib (1.0 or 1.3 mg/m^2) on Days 1, 4, 8, and 11 of a 21-day cycle utilizing four dose-escalation cohorts.

The Phase 2 portion of the study was designed to determine the preliminary efficacy of KW 2478 and Bortezomib at the RP2D (KW-2478 175 mg/m^2/Bortezomib 1.3 mg/m^2).

Arm type	Experimental

Investigational medicinal product name	KW-2478
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

175mg/m2

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.3mg/m2

Arm title	Phase 1 Cohort 1: KW-2478 130 mg/m^2 and Bortezomib 1.0mg/m^2

Arm description:

Cohort 1: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.

Arm type	Experimental
Investigational medicinal product name	KW-2478
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

130mg/m2

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.0mg/m2

Arm title	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3mg/m^2

Arm description:

Cohort 2: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.

Arm type	Experimental
Investigational medicinal product name	KW-2478
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

130mg/m2

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.3mg/m2

Arm title	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0mg/m^2

Arm description:

Cohort 3: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.

Arm type	Experimental
Investigational medicinal product name	KW-2478
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

175mg/m2

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.0mg/m2

Arm title	Phase 1 Cohort 4: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2

Arm description:

Cohort 4: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.

Arm type	Experimental
Investigational medicinal product name	KW-2478
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

175mg/m2

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.3mg/m2

Arm title	Phase 2: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2

Arm description:

Phase 2: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle designed to determine the preliminary efficacy of KW 2478 and Bortezomib at the RP2D (KW-2478 175 mg/m^2/Bortezomib 1.3 mg/m^2).

Arm type	Experimental

Investigational medicinal product name	KW-2478
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

175mg/m2

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.3mg/m2

Arm title	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3mg/m^2

Arm description:

Both agents administered on Days 1, 4, 8 and 11 of a 21 day cycle

Arm type	Experimental
Investigational medicinal product name	KW-2478
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

130mg/m2

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.3mg/m2

Arm title	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0mg/m^2

Arm description:

Cohort 3: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.

Arm type	Experimental
Investigational medicinal product name	KW-2478
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

175mg/m2

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.0mg/m2

Number of subjects in period 1	Phase 1: KW-2478 and Bortezomib	Phase II: KW-2478 130mg/m^2 and Bortezomib 1.3mg/m^2	KW-2478 and bortezomib
Started	15	80	80
Completed	15	80	6
Not completed	0	0	74
Unknown	-	-	74

Number of subjects in period 1	Phase 1 & 2: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2	Phase 1 Cohort 1: KW-2478 130 mg/m^2 and Bortezomib 1.0mg/m^2	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3mg/m^2
Started	80	3	3
Completed	6	0	0
Not completed	74	3	3
Unknown	74	3	3

Number of subjects in period 1	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0mg/m^2	Phase 1 Cohort 4: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2	Phase 2: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2
Started	3	6	80
Completed	0	0	6
Not completed	3	6	74
Unknown	3	6	74

Number of subjects in period 1	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3mg/m^2	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0mg/m^2
Started	3	3
Completed	0	0
Not completed	3	3
Unknown	3	3

Baseline characteristics

Reporting groups

Reporting group title	Phase 1: KW-2478 and Bortezomib

Reporting group description:

The target population in Phase 1 were adults (≥18 years) of either gender with a confirmed history of MM by IMWG criteria had relapsed or failed to respond to 1–3 prior MM regimens with an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 and a life expectancy ≥ 3 months. Subjects had to have disease that could be evaluated by serum or urinary levels of M protein or serum free light chains in the absence of measurable M protein in serum or urine.

For Phase 1, the design was a standard 3+3 study of KW-2478 (130 or 175 mg/m^2) and bortezomib(1.0 or 1.3 mg/m^2) on Days 1, 4, 8, and 11 of a 21-day cycle utilizing four dose-escalation

Reporting group title	Phase II: KW-2478 130mg/m^2 and Bortezomib 1.3mg/m^2

Reporting group description:

The target population in Phase 2 were adults (≥18 years) of either gender with a confirmed history of MM by IMWG criteria had relapsed or failed to respond to 1–3 prior MM regimens with an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 and a life expectancy ≥ 3 months. Subjects had to have disease that could be evaluated by serum or urinary levels of M protein or serum free light chains in the absence of measurable M protein in serum or urine.
For the Phase 2 portion of the study was designed to determine the preliminary efficacy of KW 2478 and bortezomib at the RP2D (KW-2478 175 mg/m^2/bortezomib1.3 mg/m^2).

Reporting group values	Phase 1: KW-2478 and Bortezomib	Phase II: KW-2478 130mg/m^2 and Bortezomib 1.3mg/m^2	Total
Number of subjects	15	80	95
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	41	48
From 65-84 years	8	39	47
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	65.3	64.1	
standard deviation	± 8.2	± 9.6	-
Gender, Male/Female Units: participants			
Female	4	37	41
Male	11	43	54
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	21	22
Native Hawaiian or Other Pacific Islander	0	0	0

Black or African American	3	5	8
White	10	51	61
More than one race	0	0	0
Unknown or Not Reported	1	3	4
Region of Enrollment Units: Subjects			
United States	4	14	18
Philippines	0	20	20
United Kingdom	11	46	57
Body Surface Area (BSA) Units: m^2			
arithmetic mean			
standard deviation	±	±	-

Subject analysis sets

Subject analysis set title	KW-2478 and bortezomib
Subject analysis set type	Full analysis

Subject analysis set description:

The target population in both Phase 1 and 2 were adults (≥18 years) of either gender with a confirmed history of MM by IMWG criteria had relapsed or failed to respond to 1–3 prior MM regimens with an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 and a life expectancy ≥ 3 months. Subjects had to have disease that could be evaluated by serum or urinary levels of M protein or serum free light chains in the absence of measurable M protein in serum or urine.
For Phase 1, the design was a standard 3+3 study of KW-2478 (130 or 175 mg/m^2) and Bortezomib(1.0 or 1.3 mg/m^2) on Days 1, 4, 8, and 11 of a 21-day cycle utilizing four dose-escalation cohorts (overall N=15). The Phase 2 portion of the study enrolled 80 subjects to determine the preliminary efficacy of KW 2478 and Bortezomib at the RP2D (KW-2478 175 mg/m^2 / Bortezomib 1.3

Subject analysis set title	Phase 1 & 2: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

The target population in both Phase 1 and 2 were adults (≥18 years) of either gender with a confirmed history of MM by IMWG criteria had relapsed or failed to respond to 1–3 prior MM regimens with an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 and a life expectancy ≥ 3 months. Subjects had to have disease that could be evaluated by serum or urinary levels of M protein or serum free light chains in the absence of measurable M protein in serum or urine.

The Phase 1 portion of the study was a standard 3+3 study design of KW-2478 (130 or 175 mg/m^2) and Bortezomib (1.0 or 1.3 mg/m^2) on Days 1, 4, 8, and 11 of a 21-day cycle utilizing four dose-escalation cohorts.

The Phase 2 portion of the study was designed to determine the preliminary efficacy of KW 2478 and Bortezomib at the RP2D (KW-2478 175 mg/m^2/Bortezomib 1.3 mg/m^2).

Subject analysis set title	Phase 1 Cohort 1: KW-2478 130 mg/m^2 and Bortezomib 1.0mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort 1: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.

Subject analysis set title	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort 2: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.

Subject analysis set title	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort 3: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.

Subject analysis set title	Phase 1 Cohort 4: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort 4: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.

Subject analysis set title	Phase 2: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Phase 2: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle designed to determine the preliminary efficacy of KW 2478 and Bortezomib at the RP2D (KW-2478 175 mg/m^2/Bortezomib 1.3 mg/m^2).

Subject analysis set title	Phase 1 Cohort 1: KW-2478 130 mg/m^2 and Bortezomib 1.0mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Both agents administered on Days 1, 4, 8 and 11 of a 21 day cycle

Subject analysis set title	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Both agents administered on Days 1, 4, 8 and 11 of a 21 day cycle

Subject analysis set title	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Both agents administered on Days 1, 4, 8 and 11 of a 21 day cycle

Subject analysis set title	Phase 1 Cohort 4: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Both agents administered on Days 1, 4, 8 and 11 of a 21 day cycle

Reporting group values	KW-2478 and bortezomib	Phase 1 & 2: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2	Phase 1 Cohort 1: KW-2478 130 mg/m^2 and Bortezomib 1.0mg/m^2
Number of subjects	95	95	3
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	48	48	1
From 65-84 years	47	47	2
85 years and over	0	0	0

Age Continuous Units: years			
arithmetic mean	64.3	64.3	68
standard deviation	± 9.3	± 9.3	± 5.6
Gender, Male/Female Units: participants			
Female	41	41	1
Male	54	54	2
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	22	22	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	8	8	0
White	61	61	3
More than one race	0	0	0
Unknown or Not Reported	4	4	0
Region of Enrollment Units: Subjects			
United States	18	18	1
Philippines	20	20	0
United Kingdom	57	57	2
Body Surface Area (BSA) Units: m^2			
arithmetic mean	1.87		
standard deviation	± 0.27	±	±

Reporting group values	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3mg/m^2	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0mg/m^2	Phase 1 Cohort 4: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2
Number of subjects	3	3	6
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	0	3
From 65-84 years	1	3	3
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	61	70.7	63.5
standard deviation	± 6.3	± 3.8	± 10.9
Gender, Male/Female Units: participants			
Female	0	2	1

Male	3	1	5

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	2	1
White	2	1	4
More than one race	0	0	0
Unknown or Not Reported	1	0	0
Region of Enrollment Units: Subjects			
United States	0	1	2
Philippines	0	0	0
United Kingdom	3	2	4
Body Surface Area (BSA) Units: m^2			
arithmetic mean			
standard deviation	±	±	±

Reporting group values	Phase 2: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2	Phase 1 Cohort 1: KW-2478 130 mg/m^2 and Bortezomib 1.0mg/m^2	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3mg/m^2
Number of subjects	80	3	3
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	41	1	2
From 65-84 years	39	2	1
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	64.1	68	61
standard deviation	± 9.6	± 5.6	± 6.3
Gender, Male/Female Units: participants			
Female	37	1	0
Male	43	2	3
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	21	0	0

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	5	0	0
White	51	3	2
More than one race	0	0	0
Unknown or Not Reported	3	0	1
Region of Enrollment Units: Subjects			
United States		1	0
Philippines		0	0
United Kingdom		2	3
Body Surface Area (BSA) Units: m^2			
arithmetic mean standard deviation	±	±	±

Reporting group values	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0mg/m^2	Phase 1 Cohort 4: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2	
Number of subjects	3	6	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	3	
From 65-84 years	3	3	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	70.7	63.5	
standard deviation	± 3.8	± 10.9	
Gender, Male/Female Units: participants			
Female	2	1	
Male	1	5	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	1	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	1	
White	2	4	
More than one race	0	0	
Unknown or Not Reported	1	0	
Region of Enrollment			

Units: Subjects			
United States	1	2	
Philippines	0	0	
United Kingdom	2	4	
Body Surface Area (BSA)			
Units: m^2			
arithmetic mean			
standard deviation	±	±	

End points

End points reporting groups

Reporting group title	Phase 1: KW-2478 and Bortezomib

Reporting group description:

The target population in Phase 1 were adults (≥18 years) of either gender with a confirmed history of MM by IMWG criteria had relapsed or failed to respond to 1–3 prior MM regimens with an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 and a life expectancy ≥ 3 months. Subjects had to have disease that could be evaluated by serum or urinary levels of M protein or serum free light chains in the absence of measurable M protein in serum or urine.

For Phase 1, the design was a standard 3+3 study of KW-2478 (130 or 175 mg/m^2) and bortezomib(1.0 or 1.3 mg/m^2) on Days 1, 4, 8, and 11 of a 21-day cycle utilizing four dose-escalation

Reporting group title	Phase II: KW-2478 130mg/m^2 and Bortezomib 1.3mg/m^2

Reporting group description:

The target population in Phase 2 were adults (≥18 years) of either gender with a confirmed history of MM by IMWG criteria had relapsed or failed to respond to 1–3 prior MM regimens with an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 and a life expectancy ≥ 3 months. Subjects had to have disease that could be evaluated by serum or urinary levels of M protein or serum free light chains in the absence of measurable M protein in serum or urine.
For the Phase 2 portion of the study was designed to determine the preliminary efficacy of KW 2478 and bortezomib at the RP2D (KW-2478 175 mg/m^2/bortezomib1.3 mg/m^2).

Reporting group title	KW-2478 and bortezomib

Reporting group description:

The target population in both Phase 1 and 2 were adults (≥18 years) of either gender with a confirmed history of MM by IMWG criteria had relapsed or failed to respond to 1–3 prior MM regimens with an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 and a life expectancy ≥ 3 months. Subjects had to have disease that could be evaluated by serum or urinary levels of M protein or serum free light chains in the absence of measurable M protein in serum or urine.
For Phase 1, the design was a standard 3+3 study of KW-2478 (130 or 175 mg/m^2) and Bortezomib(1.0 or 1.3 mg/m^2) on Days 1, 4, 8, and 11 of a 21-day cycle utilizing four dose-escalation cohorts (overall N=15). The Phase 2 portion of the study enrolled 80 subjects to determine the preliminary efficacy of KW 2478 and Bortezomib at the RP2D (KW-2478 175 mg/m^2 / Bortezomib 1.3

Reporting group title	Phase 1 & 2: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2

Reporting group description:

The target population in both Phase 1 and 2 were adults (≥18 years) of either gender with a confirmed history of MM by IMWG criteria had relapsed or failed to respond to 1–3 prior MM regimens with an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 and a life expectancy ≥ 3 months. Subjects had to have disease that could be evaluated by serum or urinary levels of M protein or serum free light chains in the absence of measurable M protein in serum or urine.

The Phase 1 portion of the study was a standard 3+3 study design of KW-2478 (130 or 175 mg/m^2) and Bortezomib (1.0 or 1.3 mg/m^2) on Days 1, 4, 8, and 11 of a 21-day cycle utilizing four dose-escalation cohorts.

The Phase 2 portion of the study was designed to determine the preliminary efficacy of KW 2478 and Bortezomib at the RP2D (KW-2478 175 mg/m^2/Bortezomib 1.3 mg/m^2).

Reporting group title	Phase 1 Cohort 1: KW-2478 130 mg/m^2 and Bortezomib 1.0mg/m^2

Reporting group description:

Cohort 1: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.

Reporting group title	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3mg/m^2

Reporting group description:

Cohort 2: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.

Reporting group title	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0mg/m^2

Reporting group description:

Cohort 3: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.

Reporting group title	Phase 1 Cohort 4: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2

Reporting group description:

Cohort 4: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.

Reporting group title	Phase 2: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2

Reporting group description:

Phase 2: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle designed to determine the preliminary efficacy of KW 2478 and Bortezomib at the RP2D (KW-2478 175 mg/m^2/Bortezomib 1.3 mg/m^2).

Reporting group title	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3mg/m^2

Reporting group description:

Both agents administered on Days 1, 4, 8 and 11 of a 21 day cycle

Reporting group title	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0mg/m^2

Reporting group description:

Cohort 3: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.

Subject analysis set title	KW-2478 and bortezomib
Subject analysis set type	Full analysis

Subject analysis set description:

The target population in both Phase 1 and 2 were adults (≥18 years) of either gender with a confirmed history of MM by IMWG criteria had relapsed or failed to respond to 1–3 prior MM regimens with an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 and a life expectancy ≥ 3 months. Subjects had to have disease that could be evaluated by serum or urinary levels of M protein or serum free light chains in the absence of measurable M protein in serum or urine.
For Phase 1, the design was a standard 3+3 study of KW-2478 (130 or 175 mg/m^2) and Bortezomib(1.0 or 1.3 mg/m^2) on Days 1, 4, 8, and 11 of a 21-day cycle utilizing four dose-escalation cohorts (overall N=15). The Phase 2 portion of the study enrolled 80 subjects to determine the preliminary efficacy of KW 2478 and Bortezomib at the RP2D (KW-2478 175 mg/m^2 / Bortezomib 1.3

Subject analysis set title	Phase 1 & 2: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

The target population in both Phase 1 and 2 were adults (≥18 years) of either gender with a confirmed history of MM by IMWG criteria had relapsed or failed to respond to 1–3 prior MM regimens with an Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 and a life expectancy ≥ 3 months. Subjects had to have disease that could be evaluated by serum or urinary levels of M protein or serum free light chains in the absence of measurable M protein in serum or urine.

The Phase 1 portion of the study was a standard 3+3 study design of KW-2478 (130 or 175 mg/m^2) and Bortezomib (1.0 or 1.3 mg/m^2) on Days 1, 4, 8, and 11 of a 21-day cycle utilizing four dose-escalation cohorts.

The Phase 2 portion of the study was designed to determine the preliminary efficacy of KW 2478 and Bortezomib at the RP2D (KW-2478 175 mg/m^2/Bortezomib 1.3 mg/m^2).

Subject analysis set title	Phase 1 Cohort 1: KW-2478 130 mg/m^2 and Bortezomib 1.0mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort 1: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.

Subject analysis set title	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort 2: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3

study design.

Subject analysis set title	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort 3: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.

Subject analysis set title	Phase 1 Cohort 4: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Cohort 4: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.

Subject analysis set title	Phase 2: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Phase 2: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle designed to determine the preliminary efficacy of KW 2478 and Bortezomib at the RP2D (KW-2478 175 mg/m^2/Bortezomib 1.3 mg/m^2).

Subject analysis set title	Phase 1 Cohort 1: KW-2478 130 mg/m^2 and Bortezomib 1.0mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Both agents administered on Days 1, 4, 8 and 11 of a 21 day cycle

Subject analysis set title	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Both agents administered on Days 1, 4, 8 and 11 of a 21 day cycle

Subject analysis set title	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Both agents administered on Days 1, 4, 8 and 11 of a 21 day cycle

Subject analysis set title	Phase 1 Cohort 4: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Both agents administered on Days 1, 4, 8 and 11 of a 21 day cycle

Primary: To establish the safety, tolerability, and RP2D (Phase 1); To assess the overall response rate in subjects with advanced Multiple Myeloma (Phase 2).

End point title	To establish the safety, tolerability, and RP2D (Phase 1); To assess the overall response rate in subjects with advanced Multiple Myeloma (Phase 2).[1]

End point description:

The safety of KW-2478 was determined by reported TEAEs, observed DLTs, changes in PEs, vital sign measurements, ECGs, and laboratory analyses.
The ORR, was defined as the best response over a specified number of cycles (calculated and summarized).
Disease control rate (DCR) was defined as the best response over a specified number of cycles (calculated and summarized). Progression-free survival was defined as the time from the first day of treatment until the date of disease progression or death is first reported (calculated and summarized).

End point type	Primary

End point timeframe:

21 day cycle, up to 52 weeks

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: Owing to the nonrandomized nature of this trial and the limited sample sizes involved, no formal statistical hypothesis testing was conducted. Data from all centers were pooled.
Except as otherwise specified in the SAP, missing data were not imputed.

End point values	Phase 1 & 2: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2	Phase 1 Cohort 1: KW-2478 130 mg/m^2 and Bortezomib 1.0mg/m^2	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3mg/m^2	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	95	3	3	3
Units: participants				
number (not applicable)				
Subjects with Any TEAE	95	3	3	3
Related TEAE	88	3	3	2
Moderate (CTCAE 2) TEAE	22	0	0	0
Severe (CTCAE 3) TEAE	54	3	2	2
Life Threatening TEAE	13	0	1	0
Serious Treatment-Emergent AE	48	2	3	3
Subjects with Any DLT	1	0	0	1

End point values	Phase 1 Cohort 4: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2	Phase 2: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	80		
Units: participants				
number (not applicable)				
Subjects with Any TEAE	6	80		
Related TEAE	6	74		
Moderate (CTCAE 2) TEAE	0	22		
Severe (CTCAE 3) TEAE	5	42		
Life Threatening TEAE	0	12		
Serious Treatment-Emergent AE	4	36		
Subjects with Any DLT	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: PK Absorption tmax hr Day 11

End point title	Phase 1: PK Absorption tmax hr Day 11

End point description:

Descriptive summary statistics (number, arithmetic mean, standard deviation [SDev], coefficient of variation [CV%]) for concentration and PK data for KW-2478 and Bortezomib in Phase 1 were presented by cohort, dose level and day.

End point type	Secondary

End point timeframe:

PK collected Day 11 of 21-day cycle

End point values	Phase 1 Cohort 1: KW-2478 130 mg/m^2 and Bortezomib 1.0mg/m^2	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3mg/m^2	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0mg/m^2	Phase 1 Cohort 4: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: hr				
arithmetic mean (standard deviation)	1.03 (± 0.0441)	1.03 (± 0.0481)	1.11 (± 0.129)	1.07 (± 0.0638)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: PK Exposure Cmax ng/mL Day 11

End point title	Phase 1: PK Exposure Cmax ng/mL Day 11

End point description:

Descriptive summary statistics (number, arithmetic mean, standard deviation [SDev], coefficient of variation [CV%]) for concentration and PK data for KW-2478 and Bortezomib in Phase 1 were presented by cohort, dose level and day.

End point type	Secondary

End point timeframe:

PK collected Day 11 of 21-day cycle

End point values	Phase 1 Cohort 1: KW-2478 130 mg/m^2 and Bortezomib 1.0mg/m^2	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3mg/m^2	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0mg/m^2	Phase 1 Cohort 4: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: ng/mL				
arithmetic mean (standard deviation)	7910 (± 5360)	41000 (± 64100)	5990 (± 2720)	5280 (± 2290)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: PK Exposure AUC0-t hr*ng/mL Day 11

End point title	Phase 1: PK Exposure AUC0-t hr*ng/mL Day 11

End point description:

Descriptive summary statistics (number, arithmetic mean, standard deviation [SDev], coefficient of variation [CV%]) for concentration and PK data for KW-2478 and Bortezomib in Phase 1 were presented by cohort, dose level and day.

End point type	Secondary

End point timeframe:

PK collected Day 11 of 21-day cycle

End point values	Phase 1 Cohort 1: KW-2478 130 mg/m^2 and Bortezomib 1.0mg/m^2	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3mg/m^2	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0mg/m^2	Phase 1 Cohort 4: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: hr*ng/mL				
arithmetic mean (standard deviation)	7940 (± 2580)	26200 (± 36700)	7190 (± 2150)	6040 (± 2280)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: PK Elimination t½ hr Day 11

End point title	Phase 1: PK Elimination t½ hr Day 11

End point description:

Descriptive summary statistics (number, arithmetic mean, standard deviation [SDev], coefficient of variation [CV%]) for concentration and PK data for KW-2478 and Bortezomib in Phase 1 were presented by cohort, dose level and day.

End point type	Secondary

End point timeframe:

PK collected Day 11 of 21-day cycle

End point values	Phase 1 Cohort 1: KW-2478 130 mg/m^2 and Bortezomib 1.0mg/m^2	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3mg/m^2	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0mg/m^2	Phase 1 Cohort 4: KW-2478 175 mg/m^2 and Bortezomib 1.3mg/m^2
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	6
Units: hr				
arithmetic mean (standard deviation)	1.88 (± 0.076)	2.02 (± 0)	1.84 (± 0.206)	1.77 (± 0.262)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Throughout study	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups	
Reporting group title	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3 mg/m^2
Reporting group description:	
Cohort 2: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.	
Reporting group title	Phase 1 and 2: KW-2478 and bortezomib
Reporting group description:	
KW-2478 and bortezomib: KW 2478 and bortezomib given on Days 1, 4, 8 and 11 of a 21 day cycle	
Reporting group title	Phase 1 Cohort 1: KW-2478 130 mg/m^2 and Bortezomib 1.0 mg/m^2
Reporting group description:	
Cohort 1: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.	
Reporting group title	Phase 1 Cohort 4: KW-2478 175 mg/m^2 and Bortezomib 1.3 mg/m^2
Reporting group description:	
Cohort 4: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.	
Reporting group title	Phase 2: KW-2478 175 mg/m^2 and Bortezomib 1.3 mg/m^2
Reporting group description:	
Phase 2: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle designed to determine the preliminary efficacy of KW 2478 + BTZ at the RP2D (KW-2478 175 mg/m^2/BTZ 1.3 mg/m^2).	
Reporting group title	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0 mg/m^2
Reporting group description:	
Cohort 3: Both agents administered on Days 1, 4, 8, and 11 of a 21-day cycle with a standard 3+3 study design.	

Serious adverse events	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3 mg/m^2	Phase 1 and 2: KW-2478 and bortezomib	Phase 1 Cohort 1: KW-2478 130 mg/m^2 and Bortezomib 1.0 mg/m^2
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	48 / 95 (50.53%)	2 / 3 (66.67%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Multiple myeloma			

subjects affected / exposed	1 / 3 (33.33%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	4 / 95 (4.21%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			

subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin T increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Viral test positive			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Weight decreased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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

Clavicle fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Fall			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Hip fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Angina unstable			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Myocardial ischaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Right ventricular failure			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Nervous system disorders			

Loss of consciousness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Neuropathy peripheral			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Transient ischaemic attack			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	4 / 95 (4.21%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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

Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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 / 3 (0.00%)	1 / 95 (1.05%)	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
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	4 / 95 (4.21%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Pancreatitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Rash erythematous			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Neurogenic bladder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Musculoskeletal chest pain			

subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	1 / 3 (33.33%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Catheter sepsis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Listeriosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Lower respiratory tract infection			

subjects affected / exposed	0 / 3 (0.00%)	4 / 95 (4.21%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Lung infection pseudomonal			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	7 / 95 (7.37%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Urinary tract infection			

subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	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
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 1 Cohort 4: KW-2478 175 mg/m^2 and Bortezomib 1.3 mg/m^2	Phase 2: KW-2478 175 mg/m^2 and Bortezomib 1.3 mg/m^2	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0 mg/m^2
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	36 / 80 (45.00%)	3 / 3 (100.00%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Multiple myeloma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (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
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
General disorders and administration site conditions			

Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (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
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (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
Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin T increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (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
Viral test positive			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (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			
Accidental overdose			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Clavicle fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (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
Fall			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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

Hip fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (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			
Angina pectoris			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (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
Angina unstable			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Myocardial ischaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Right ventricular failure			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Neuropathy peripheral			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	1 / 6 (16.67%)	0 / 80 (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

Transient ischaemic attack			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	4 / 80 (5.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 6 (16.67%)	0 / 80 (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
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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 / 6 (0.00%)	1 / 80 (1.25%)	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
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Pancreatitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 80 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash erythematous			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Neurogenic bladder			

subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Infections and infestations			
Appendicitis			

subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Bacteraemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Catheter sepsis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Listeriosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Lower respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Lung infection pseudomonal			

subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Pneumonia			
subjects affected / exposed	1 / 6 (16.67%)	6 / 80 (7.50%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (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
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			

subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	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
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Phase 1 Cohort 2: KW-2478 130 mg/m^2 and Bortezomib 1.3 mg/m^2	Phase 1 and 2: KW-2478 and bortezomib	Phase 1 Cohort 1: KW-2478 130 mg/m^2 and Bortezomib 1.0 mg/m^2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	95 / 95 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	5 / 95 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	9	0
Orthostatic hypotension			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	3	0

Phlebitis			
subjects affected / exposed	0 / 3 (0.00%)	4 / 95 (4.21%)	1 / 3 (33.33%)
occurrences (all)	0	5	1
Thrombophlebitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Vasculitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Vein discolouration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	15 / 95 (15.79%)	0 / 3 (0.00%)
occurrences (all)	0	17	0
Catheter site erythema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Catheter site haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Catheter site pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Catheter site related reaction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Catheter thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Chest pain			

subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Chills			
subjects affected / exposed	1 / 3 (33.33%)	4 / 95 (4.21%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Cyst			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Facial pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	3 / 3 (100.00%)	51 / 95 (53.68%)	2 / 3 (66.67%)
occurrences (all)	10	101	6
Feeling cold			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Gait disturbance			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Infusion site haematoma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Infusion site pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Injection site haematoma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Irritability			

subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	4 / 95 (4.21%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Mass			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Mucosal inflammation			
subjects affected / exposed	1 / 3 (33.33%)	4 / 95 (4.21%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Oedema peripheral			
subjects affected / exposed	1 / 3 (33.33%)	12 / 95 (12.63%)	1 / 3 (33.33%)
occurrences (all)	2	17	2
Pain			
subjects affected / exposed	0 / 3 (0.00%)	4 / 95 (4.21%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	12 / 95 (12.63%)	0 / 3 (0.00%)
occurrences (all)	2	15	0
Swelling			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			

Breast pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Epididymitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Genital pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Testicular cyst			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Testicular pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	2 / 3 (66.67%)	21 / 95 (22.11%)	1 / 3 (33.33%)
occurrences (all)	2	29	1
Dry throat			
subjects affected / exposed	1 / 3 (33.33%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Dysphonia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	19 / 95 (20.00%)	2 / 3 (66.67%)
occurrences (all)	5	25	2
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	6 / 95 (6.32%)	1 / 3 (33.33%)
occurrences (all)	0	9	2
Emphysema			

subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	8 / 95 (8.42%)	0 / 3 (0.00%)
occurrences (all)	0	9	0
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	1 / 3 (33.33%)
occurrences (all)	0	3	3
Hiccups			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Hypoxia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	1 / 3 (33.33%)	11 / 95 (11.58%)	1 / 3 (33.33%)
occurrences (all)	1	11	1
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pneumothorax			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	6 / 95 (6.32%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Pulmonary oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rales			
subjects affected / exposed	1 / 3 (33.33%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Rhinorrhoea			

subjects affected / exposed	1 / 3 (33.33%)	6 / 95 (6.32%)	0 / 3 (0.00%)
occurrences (all)	1	7	0
Sinus congestion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	1 / 3 (33.33%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	5 / 95 (5.26%)	1 / 3 (33.33%)
occurrences (all)	0	5	1
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Depressed mood			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Depression			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Insomnia			
subjects affected / exposed	1 / 3 (33.33%)	13 / 95 (13.68%)	0 / 3 (0.00%)
occurrences (all)	1	15	0
Libido decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Mood altered			
subjects affected / exposed	1 / 3 (33.33%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Nightmare			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	1 / 3 (33.33%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Blood magnesium decreased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Blood potassium decreased			
subjects affected / exposed	1 / 3 (33.33%)	4 / 95 (4.21%)	0 / 3 (0.00%)
occurrences (all)	2	5	0
Blood pressure increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood sodium decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood triglycerides increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Body temperature increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
C-reactive protein increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram QT prolonged			

subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Eosinophil count increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Haemoglobin decreased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Heart rate decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	5 / 95 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	11	0
Neutrophil count increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Protein total increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	1 / 3 (33.33%)	9 / 95 (9.47%)	0 / 3 (0.00%)
occurrences (all)	1	10	0
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	4 / 95 (4.21%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Fall			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Human bite			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Medical device site reaction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Narcotic intoxication			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Post-traumatic pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rib fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Road traffic accident			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Thermal burn			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tooth fracture			

subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Extrasystoles			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Areflexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Balance disorder			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Burning sensation			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Depressed level of consciousness			
subjects affected / exposed	1 / 3 (33.33%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Dizziness			

subjects affected / exposed	0 / 3 (0.00%)	25 / 95 (26.32%)	3 / 3 (100.00%)
occurrences (all)	0	33	8
Dizziness exertional			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Dysgeusia			
subjects affected / exposed	1 / 3 (33.33%)	13 / 95 (13.68%)	2 / 3 (66.67%)
occurrences (all)	1	13	2
Head discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	23 / 95 (24.21%)	1 / 3 (33.33%)
occurrences (all)	0	41	1
Hyperaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyperreflexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia			
subjects affected / exposed	2 / 3 (66.67%)	8 / 95 (8.42%)	0 / 3 (0.00%)
occurrences (all)	3	11	0
Hypogeusia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyporeflexia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	2	3	0
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)	6 / 95 (6.32%)	0 / 3 (0.00%)
occurrences (all)	0	8	0
Memory impairment			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Neuralgia			

subjects affected / exposed	0 / 3 (0.00%)	8 / 95 (8.42%)	0 / 3 (0.00%)
occurrences (all)	0	13	0
Neuropathy peripheral			
subjects affected / exposed	2 / 3 (66.67%)	28 / 95 (29.47%)	1 / 3 (33.33%)
occurrences (all)	3	48	1
Paraesthesia			
subjects affected / exposed	2 / 3 (66.67%)	11 / 95 (11.58%)	0 / 3 (0.00%)
occurrences (all)	5	17	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	15 / 95 (15.79%)	1 / 3 (33.33%)
occurrences (all)	0	36	1
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Sensory loss			
subjects affected / exposed	1 / 3 (33.33%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	2	3	0
Somnolence			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	2 / 3 (66.67%)
occurrences (all)	0	4	3
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	17 / 95 (17.89%)	0 / 3 (0.00%)
occurrences (all)	0	30	0
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Leukocytosis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0

Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	1 / 3 (33.33%)	15 / 95 (15.79%)	0 / 3 (0.00%)
occurrences (all)	1	37	0
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	19 / 95 (20.00%)	0 / 3 (0.00%)
occurrences (all)	0	41	0
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ear discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ear pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tinnitus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	1 / 3 (33.33%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Eye disorders			
Abnormal sensation in eye			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Blepharitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Conjunctival hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			

subjects affected / exposed	0 / 3 (0.00%)	4 / 95 (4.21%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Diplopia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	4 / 95 (4.21%)	1 / 3 (33.33%)
occurrences (all)	0	4	1
Erythema of eyelid			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Eye discharge			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	1 / 3 (33.33%)
occurrences (all)	0	3	1
Eye irritation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eye pain			
subjects affected / exposed	0 / 3 (0.00%)	4 / 95 (4.21%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Eye pruritus			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Eye swelling			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eyelid disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eyelid oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eyelids pruritus			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Foreign body sensation in eyes			

subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Lacrimation increased			
subjects affected / exposed	0 / 3 (0.00%)	12 / 95 (12.63%)	1 / 3 (33.33%)
occurrences (all)	0	15	1
Macular degeneration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Metamorphopsia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ocular hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Photophobia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Retinal disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	16 / 95 (16.84%)	1 / 3 (33.33%)
occurrences (all)	0	19	1
Visual acuity reduced			
subjects affected / exposed	1 / 3 (33.33%)	4 / 95 (4.21%)	0 / 3 (0.00%)
occurrences (all)	1	5	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	5 / 95 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	13 / 95 (13.68%)	2 / 3 (66.67%)
occurrences (all)	0	19	6
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	17 / 95 (17.89%)	2 / 3 (66.67%)
occurrences (all)	0	31	5

Abdominal pain lower			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	11 / 95 (11.58%)	3 / 3 (100.00%)
occurrences (all)	0	12	3
Abdominal tenderness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Anal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	2 / 3 (66.67%)	42 / 95 (44.21%)	3 / 3 (100.00%)
occurrences (all)	4	71	8
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)	70 / 95 (73.68%)	3 / 3 (100.00%)
occurrences (all)	9	199	29
Dry mouth			
subjects affected / exposed	1 / 3 (33.33%)	7 / 95 (7.37%)	0 / 3 (0.00%)
occurrences (all)	1	7	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	13 / 95 (13.68%)	2 / 3 (66.67%)
occurrences (all)	0	20	3
Dysphagia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	1 / 3 (33.33%)
occurrences (all)	0	5	3
Frequent bowel movements			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	2	0

Gastrointestinal hypermotility			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Gingival pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gingivitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Glossodynia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Haemorrhoids			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Irritable bowel syndrome			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Mouth ulceration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	55 / 95 (57.89%)	3 / 3 (100.00%)
occurrences (all)	2	114	11
Oral pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Pneumatosis intestinalis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Proctalgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tongue coated			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	38 / 95 (40.00%)	1 / 3 (33.33%)
occurrences (all)	3	72	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dermatitis allergic			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dry skin			
subjects affected / exposed	1 / 3 (33.33%)	7 / 95 (7.37%)	0 / 3 (0.00%)
occurrences (all)	1	7	0
Ecchymosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	4 / 95 (4.21%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Exfoliative rash			

subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ingrowing nail			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pain of skin			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 3 (33.33%)	8 / 95 (8.42%)	0 / 3 (0.00%)
occurrences (all)	1	9	0
Pruritus generalised			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Purpura			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	13 / 95 (13.68%)	0 / 3 (0.00%)
occurrences (all)	0	17	0
Rash erythematous			
subjects affected / exposed	0 / 3 (0.00%)	4 / 95 (4.21%)	1 / 3 (33.33%)
occurrences (all)	0	4	1
Rash macular			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rash papular			

subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rash pruritic			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Skin disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin lesion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Subcutaneous nodule			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Telangiectasia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Renal failure			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Renal impairment			
subjects affected / exposed	1 / 3 (33.33%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	1	4	0

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	12 / 95 (12.63%)	0 / 3 (0.00%)
occurrences (all)	0	15	0
Back pain			
subjects affected / exposed	1 / 3 (33.33%)	12 / 95 (12.63%)	0 / 3 (0.00%)
occurrences (all)	1	13	0
Bone disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	5 / 95 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Coccydynia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dactylitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Fasciitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Groin pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Joint range of motion decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Joint stiffness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Joint swelling			

subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Limb discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Mobility decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	10 / 95 (10.53%)	0 / 3 (0.00%)
occurrences (all)	0	13	0
Muscle twitching			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	4 / 95 (4.21%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 3 (33.33%)	10 / 95 (10.53%)	0 / 3 (0.00%)
occurrences (all)	1	10	0
Musculoskeletal pain			
subjects affected / exposed	1 / 3 (33.33%)	12 / 95 (12.63%)	0 / 3 (0.00%)
occurrences (all)	1	17	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	5 / 95 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Neck pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	15 / 95 (15.79%)	0 / 3 (0.00%)
occurrences (all)	0	19	0
Pain in jaw			

subjects affected / exposed	1 / 3 (33.33%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	2	3	0
Rheumatoid arthritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Spinal osteoarthritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchiectasis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis infective			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Enterocolitis infectious			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Escherichia urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eye infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Eyelid infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Gingival infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hordeolum			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Infection			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Localised infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	1 / 3 (33.33%)	14 / 95 (14.74%)	2 / 3 (66.67%)
occurrences (all)	1	19	4
Lung infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	7 / 95 (7.37%)	0 / 3 (0.00%)
occurrences (all)	0	8	0
Onychomycosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Orchitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	1 / 3 (33.33%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Rhinitis			
subjects affected / exposed	1 / 3 (33.33%)	7 / 95 (7.37%)	0 / 3 (0.00%)
occurrences (all)	3	13	0
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Skin candida			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin infection			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	14 / 95 (14.74%)	1 / 3 (33.33%)
occurrences (all)	0	15	1
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	6 / 95 (6.32%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Viral infection			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	3	0

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 3 (0.00%)	28 / 95 (29.47%)	2 / 3 (66.67%)
occurrences (all)	0	44	4
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	6 / 95 (6.32%)	1 / 3 (33.33%)
occurrences (all)	0	6	1
Diabetes mellitus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Fluid intake reduced			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Fluid overload			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gout			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyperphosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			

subjects affected / exposed	0 / 3 (0.00%)	5 / 95 (5.26%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Hypoglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)	8 / 95 (8.42%)	0 / 3 (0.00%)
occurrences (all)	1	13	0
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	4 / 95 (4.21%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 95 (3.16%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 95 (2.11%)	0 / 3 (0.00%)
occurrences (all)	0	10	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 3 (0.00%)	1 / 95 (1.05%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Phase 1 Cohort 4: KW-2478 175 mg/m^2 and Bortezomib 1.3 mg/m^2	Phase 2: KW-2478 175 mg/m^2 and Bortezomib 1.3 mg/m^2	Phase 1 Cohort 3: KW-2478 175 mg/m^2 and Bortezomib 1.0 mg/m^2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	80 / 80 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hot flush			

subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	5 / 80 (6.25%)	0 / 3 (0.00%)
occurrences (all)	0	9	0
Orthostatic hypotension			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Phlebitis			
subjects affected / exposed	1 / 6 (16.67%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Thrombophlebitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Vasculitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Vein discolouration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 6 (33.33%)	13 / 80 (16.25%)	0 / 3 (0.00%)
occurrences (all)	2	15	0
Catheter site erythema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Catheter site haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Catheter site pain			

subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Catheter site related reaction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Catheter thrombosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Chest discomfort			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	1 / 3 (33.33%)
occurrences (all)	0	2	2
Chills			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Cyst			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Facial pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	3 / 6 (50.00%)	41 / 80 (51.25%)	2 / 3 (66.67%)
occurrences (all)	4	79	2
Feeling cold			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Gait disturbance			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Influenza like illness			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Infusion related reaction			

subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Infusion site haematoma			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Infusion site pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Injection site haematoma			
subjects affected / exposed	1 / 6 (16.67%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Irritability			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	4 / 80 (5.00%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Mass			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Mucosal inflammation			
subjects affected / exposed	1 / 6 (16.67%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	9 / 80 (11.25%)	1 / 3 (33.33%)
occurrences (all)	0	12	1
Pain			
subjects affected / exposed	0 / 6 (0.00%)	4 / 80 (5.00%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	10 / 80 (12.50%)	1 / 3 (33.33%)
occurrences (all)	0	11	2
Swelling			

subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Epididymitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Genital pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Testicular cyst			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Testicular pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	1 / 6 (16.67%)	16 / 80 (20.00%)	1 / 3 (33.33%)
occurrences (all)	1	23	2
Dry throat			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dysphonia			

subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	13 / 80 (16.25%)	2 / 3 (66.67%)
occurrences (all)	2	14	2
Dyspnoea exertional			
subjects affected / exposed	0 / 6 (0.00%)	4 / 80 (5.00%)	1 / 3 (33.33%)
occurrences (all)	0	6	1
Emphysema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	8 / 80 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	9	0
Haemoptysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hiccups			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	9 / 80 (11.25%)	0 / 3 (0.00%)
occurrences (all)	0	9	0
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pneumothorax			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Productive cough			

subjects affected / exposed	0 / 6 (0.00%)	6 / 80 (7.50%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Pulmonary oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rales			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Rhinorrhoea			
subjects affected / exposed	2 / 6 (33.33%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	2	4	0
Sinus congestion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	4 / 80 (5.00%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Depressed mood			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Depression			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Insomnia			
subjects affected / exposed	1 / 6 (16.67%)	10 / 80 (12.50%)	1 / 3 (33.33%)
occurrences (all)	1	12	1

Libido decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Mood altered			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nightmare			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Blood magnesium decreased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Blood potassium decreased			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Blood pressure increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood sodium decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood triglycerides increased			

subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Body temperature increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
C-reactive protein increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Eosinophil count increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Haemoglobin decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	1 / 3 (33.33%)
occurrences (all)	0	1	2
Heart rate decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)	4 / 80 (5.00%)	1 / 3 (33.33%)
occurrences (all)	0	10	1
Neutrophil count increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Protein total increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Weight decreased			
subjects affected / exposed	1 / 6 (16.67%)	7 / 80 (8.75%)	0 / 3 (0.00%)
occurrences (all)	2	7	0
Weight increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	4 / 80 (5.00%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Fall			
subjects affected / exposed	1 / 6 (16.67%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Human bite			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Medical device site reaction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Narcotic intoxication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Post-traumatic pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rib fracture			

subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Road traffic accident			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Thermal burn			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tooth fracture			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Extrasystoles			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	1 / 6 (16.67%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	1 / 3 (33.33%)
occurrences (all)	0	1	3
Ventricular extrasystoles			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Areflexia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Balance disorder			

subjects affected / exposed	1 / 6 (16.67%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Burning sensation			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Depressed level of consciousness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	3 / 6 (50.00%)	18 / 80 (22.50%)	1 / 3 (33.33%)
occurrences (all)	3	21	1
Dizziness exertional			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)	10 / 80 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	10	0
Head discomfort			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	2 / 6 (33.33%)	20 / 80 (25.00%)	0 / 3 (0.00%)
occurrences (all)	2	38	0
Hyperaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyperreflexia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia			
subjects affected / exposed	1 / 6 (16.67%)	5 / 80 (6.25%)	0 / 3 (0.00%)
occurrences (all)	1	7	0
Hypogeusia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyporeflexia			

subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lethargy			
subjects affected / exposed	0 / 6 (0.00%)	6 / 80 (7.50%)	0 / 3 (0.00%)
occurrences (all)	0	8	0
Memory impairment			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Neuralgia			
subjects affected / exposed	0 / 6 (0.00%)	8 / 80 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	13	0
Neuropathy peripheral			
subjects affected / exposed	0 / 6 (0.00%)	24 / 80 (30.00%)	1 / 3 (33.33%)
occurrences (all)	0	42	2
Paraesthesia			
subjects affected / exposed	1 / 6 (16.67%)	7 / 80 (8.75%)	1 / 3 (33.33%)
occurrences (all)	1	9	2
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 6 (0.00%)	14 / 80 (17.50%)	0 / 3 (0.00%)
occurrences (all)	0	35	0
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Sensory loss			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 6 (16.67%)	14 / 80 (17.50%)	2 / 3 (66.67%)
occurrences (all)	1	27	2
Febrile neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Leukocytosis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Leukopenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	14 / 80 (17.50%)	0 / 3 (0.00%)
occurrences (all)	0	36	0
Thrombocytopenia			
subjects affected / exposed	2 / 6 (33.33%)	17 / 80 (21.25%)	0 / 3 (0.00%)
occurrences (all)	2	39	0
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ear discomfort			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ear pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tinnitus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			

Abnormal sensation in eye			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blepharitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Conjunctival hyperaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	4 / 80 (5.00%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Diplopia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Erythema of eyelid			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Eye discharge			
subjects affected / exposed	1 / 6 (16.67%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Eye irritation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eye pain			
subjects affected / exposed	0 / 6 (0.00%)	4 / 80 (5.00%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Eye pruritus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eye swelling			
subjects affected / exposed	1 / 6 (16.67%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Eyelid disorder			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eyelid oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eyelids pruritus			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Foreign body sensation in eyes			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Lacrimation increased			
subjects affected / exposed	1 / 6 (16.67%)	8 / 80 (10.00%)	2 / 3 (66.67%)
occurrences (all)	1	10	3
Macular degeneration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Metamorphopsia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Photophobia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Retinal disorder			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	2 / 6 (33.33%)	12 / 80 (15.00%)	1 / 3 (33.33%)
occurrences (all)	2	15	1
Visual acuity reduced			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	4	0

Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	5 / 80 (6.25%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	9 / 80 (11.25%)	2 / 3 (66.67%)
occurrences (all)	0	11	2
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	13 / 80 (16.25%)	1 / 3 (33.33%)
occurrences (all)	4	21	1
Abdominal pain lower			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	8 / 80 (10.00%)	0 / 3 (0.00%)
occurrences (all)	0	9	0
Abdominal tenderness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Anal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	2 / 6 (33.33%)	33 / 80 (41.25%)	2 / 3 (66.67%)
occurrences (all)	3	54	2
Diarrhoea			
subjects affected / exposed	4 / 6 (66.67%)	58 / 80 (72.50%)	3 / 3 (100.00%)
occurrences (all)	6	148	7
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	6 / 80 (7.50%)	0 / 3 (0.00%)
occurrences (all)	0	6	0
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	10 / 80 (12.50%)	1 / 3 (33.33%)
occurrences (all)	0	16	1
Dysphagia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	1 / 6 (16.67%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Frequent bowel movements			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal hypermotility			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Gingival pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gingivitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Glossodynia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Haematochezia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Haemorrhoids			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Irritable bowel syndrome			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Mouth ulceration			

subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	5 / 6 (83.33%)	45 / 80 (56.25%)	1 / 3 (33.33%)
occurrences (all)	6	93	2
Oral pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Pneumatosis intestinalis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Proctalgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rectal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tongue coated			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	35 / 80 (43.75%)	1 / 3 (33.33%)
occurrences (all)	0	67	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dermatitis allergic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Dry skin			
subjects affected / exposed	0 / 6 (0.00%)	5 / 80 (6.25%)	1 / 3 (33.33%)
occurrences (all)	0	5	1
Ecchymosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	1 / 3 (33.33%)
occurrences (all)	0	4	1
Exfoliative rash			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ingrowing nail			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pain of skin			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	7 / 80 (8.75%)	0 / 3 (0.00%)
occurrences (all)	0	8	0
Pruritus generalised			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Purpura			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	2 / 6 (33.33%)	11 / 80 (13.75%)	0 / 3 (0.00%)
occurrences (all)	5	12	0

Rash erythematous			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Rash macular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rash papular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rash pruritic			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Skin disorder			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin lesion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Subcutaneous nodule			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Telangiectasia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Haematuria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Pollakiuria			

subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Proteinuria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Renal failure			
subjects affected / exposed	1 / 6 (16.67%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Renal impairment			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	11 / 80 (13.75%)	1 / 3 (33.33%)
occurrences (all)	0	14	1
Back pain			
subjects affected / exposed	1 / 6 (16.67%)	10 / 80 (12.50%)	0 / 3 (0.00%)
occurrences (all)	1	11	0
Bone disorder			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	4 / 80 (5.00%)	1 / 3 (33.33%)
occurrences (all)	0	4	2
Coccydynia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dactylitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Fasciitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Flank pain			

subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Groin pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint range of motion decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Joint stiffness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Limb discomfort			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Mobility decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	10 / 80 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	13	0
Muscle twitching			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	4 / 80 (5.00%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 6 (16.67%)	7 / 80 (8.75%)	1 / 3 (33.33%)
occurrences (all)	1	7	1
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	10 / 80 (12.50%)	1 / 3 (33.33%)
occurrences (all)	0	15	1
Musculoskeletal stiffness			

subjects affected / exposed	1 / 6 (16.67%)	1 / 80 (1.25%)	1 / 3 (33.33%)
occurrences (all)	1	2	1
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	4 / 80 (5.00%)	1 / 3 (33.33%)
occurrences (all)	0	4	2
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Pain in extremity			
subjects affected / exposed	1 / 6 (16.67%)	13 / 80 (16.25%)	1 / 3 (33.33%)
occurrences (all)	1	17	1
Pain in jaw			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rheumatoid arthritis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Spinal osteoarthritis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchiectasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis infective			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Cystitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Enterocolitis infectious			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eye infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eyelid infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingival infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hordeolum			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Localised infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Lower respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	11 / 80 (13.75%)	0 / 3 (0.00%)
occurrences (all)	0	14	0
Lung infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	7 / 80 (8.75%)	0 / 3 (0.00%)
occurrences (all)	0	8	0
Onychomycosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	1 / 6 (16.67%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Orchitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Rhinitis			
subjects affected / exposed	0 / 6 (0.00%)	6 / 80 (7.50%)	0 / 3 (0.00%)
occurrences (all)	0	10	0
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Skin candida			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Skin infection			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	13 / 80 (16.25%)	0 / 3 (0.00%)
occurrences (all)	0	14	0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	5 / 80 (6.25%)	1 / 3 (33.33%)
occurrences (all)	0	6	1
Viral infection			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 6 (16.67%)	25 / 80 (31.25%)	0 / 3 (0.00%)
occurrences (all)	2	38	0
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	5 / 80 (6.25%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Diabetes mellitus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fluid intake reduced			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Fluid overload			
subjects affected / exposed	1 / 6 (16.67%)	0 / 80 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gout			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypercalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Hyperglycaemia			

subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyperphosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hyperuricaemia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	5 / 80 (6.25%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	7 / 80 (8.75%)	0 / 3 (0.00%)
occurrences (all)	0	12	0
Hypomagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)	4 / 80 (5.00%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 80 (3.75%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Hypophosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 80 (2.50%)	0 / 3 (0.00%)
occurrences (all)	0	10	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 6 (0.00%)	1 / 80 (1.25%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 December 2009	Operational and background information for the new sites in the Philippines.
21 December 2010	• Added investigational sites in the Philippines for the Phase 2 portion of the study. • Clarified the inclusion and exclusion criteria for the intended subject population. • Defined the period of time that subjects could continue to receive combination therapy with KW-2478 and BTZ and specified treatment with single-agent KW-2478 after discontinuation of BTZ. • Clarified wording for study drug administration and subsequent dose modifications. • Defined the Efficacy Analysis population. • Documented the change in sponsorship.
19 April 2012	• Clarified the inclusion and exclusion criteria for the intended subject population. • Clarified intended wording regarding the administration of the investigational products and subsequent dose modifications. • Clarified laboratory testing parameters and laboratory facilities responsible for the analysis of samples. • Clarified para proteins included in the quantitative determination of immunoglobulins for efficacy evaluation. • Clarified study procedures. • Clarified IMWG response criteria and criteria for progressive disease per current literature. • Updated study drug information relative to new formulation of investigational product.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported