



Clinical trial results:

A phase Ib/II study of LEE011 in combination with fulvestrant and BYL719 or BKM120 in the treatment of postmenopausal women with hormone receptor positive, HER2 negative locally recurrent or advanced metastatic breast cancer

Summary

EudraCT number	2013-004587-65
Trial protocol	IT GB
Global end of trial date	17 April 2018

Results information

Result version number	v1 (current)
This version publication date	24 April 2019
First version publication date	24 April 2019

Trial information

Trial identification

Sponsor protocol code	CLEE011X2108
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02088684
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.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	17 April 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 April 2018
Global end of trial reached?	Yes
Global end of trial date	17 April 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The Primary objective for this trial was to estimate the Maximum Tolerated Dose (MTD) and/or Recommended Phase II Dose (RP2D) and schedule of the following two combinations in patients with HR-positive/HER2-negative advanced BC.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 May 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Korea, Republic of: 2
Country: Number of subjects enrolled	Singapore: 10
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Taiwan: 8
Country: Number of subjects enrolled	United States: 34
Worldwide total number of subjects	70
EEA total number of subjects	16

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)	49
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Novartis made the decision to not open the Phase II portion of the study, for business reasons. Sufficient data had already been collected and no additional data for the triplet combinations was needed. As a result, the Phase II portion of the trial was not opened. Investigators continued to complete the Phase I portion per Amendment 3.

Pre-assignment

Screening details:

Full Analysis set and safety set both include 70 patients
Dose determining set includes 64 patients
Pharmacokinetic set includes 68 patients

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	LEE011 600 mg + fulvestrant

Arm description:

LEE011 - 28 day cycles (3 weeks on, 1 week off), fulvestrant - 500 mg i.m. given on Day 1 and Day 15 of Cycle 1, then on Day 1 of each subsequent cycle.

Arm type	escalation cohort, experimental dosing
Investigational medicinal product name	LEE011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

600 mg, 3 weeks on 1 week off

Arm title	LEE011 continuous 400mg cont. + fulvestrant
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Arm description:

LEE011 + fulvestrant Edit LEE011 - 28 day cycles (continuous daily dosing - dose escalating) fulvestrant - 500 mg i.m. given on Day 1 and Day 15 of Cycle 1, then on Day 1 of each subsequent cycle.

Arm type	escalation cohort, experimental dosing
Investigational medicinal product name	LEE011
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

400 mg continuous

Arm title	LEE011 + BYL719 + fulvestrant
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Arm description:

LEE011 - 28 day cycles (21 days followed by a 7 day break - dose escalating) BYL719 - daily (dose escalating) fulvestrant - i.m. - 500 mg given on day 1 and day 15 of Cycle 1, then on Day 1 of each subsequent cycle.

Arm type	escalation cohort, experimental dosing
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Investigational medicinal product name	BYL719
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Buccal tablet
Routes of administration	Oral use
Dosage and administration details:	
50 and 200 mg	
Arm title	LEE011 + BKM120 + fulvestrant

Arm description:

LEE011 - 28 day cycles (21 days followed by a 7 day break - dose escalating) BKM120 - daily (dose escalating) fulvestrant - i.m. - 500 mg given on day 1 and day 15 of Cycle 1, then on Day 1 of each subsequent cycle.

Arm type	escalation cohort, experimental dosing
Investigational medicinal product name	BKM120
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

10 and 50 mg

Number of subjects in period 1	LEE011 600 mg + fulvestrant	LEE011 continuous 400mg cont. + fulvestrant	LEE011 + BYL719 + fulvestrant
Started	13	15	18
Completed	0	2	1
Not completed	13	13	17
Physician decision	1	2	-
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	1	2	4
progressive disease	11	9	12

Number of subjects in period 1	LEE011 + BKM120 + fulvestrant
Started	24
Completed	3
Not completed	21
Physician decision	-
Consent withdrawn by subject	2
Adverse event, non-fatal	2
progressive disease	17

Baseline characteristics

Reporting groups

Reporting group title	LEE011 600 mg + fulvestrant
Reporting group description: LEE011 - 28 day cycles (3 weeks on, 1 week off), fulvestrant - 500 mg i.m. given on Day 1 and Day 15 of Cycle 1, then on Day 1 of each subsequent cycle.	
Reporting group title	LEE011 continuous 400mg cont. + fulvestrant
Reporting group description: LEE011 + fulvestrant Edit LEE011 - 28 day cycles (continuous daily dosing - dose escalating) fulvestrant - 500 mg i.m. given on Day 1 and Day 15 of Cycle 1, then on Day 1 of each subsequent cycle.	
Reporting group title	LEE011 + BYL719 + fulvestrant
Reporting group description: LEE011 - 28 day cycles (21 days followed by a 7 day break - dose escalating) BYL719 - daily (dose escalating) fulvestrant - i.m. - 500 mg given on day 1 and day 15 of Cycle 1, then on Day 1 of each subsequent cycle.	
Reporting group title	LEE011 + BKM120 + fulvestrant
Reporting group description: LEE011 - 28 day cycles (21 days followed by a 7 day break - dose escalating) BKM120 - daily (dose escalating) fulvestrant - i.m. - 500 mg given on day 1 and day 15 of Cycle 1, then on Day 1 of each subsequent cycle.	

Reporting group values	LEE011 600 mg + fulvestrant	LEE011 continuous 400mg cont. + fulvestrant	LEE011 + BYL719 + fulvestrant
Number of subjects	13	15	18
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)	8	11	11
From 65-84 years	5	4	7
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	59.5	57.5	60.3
standard deviation	± 8.02	± 8.81	± 11.69
Sex: Female, Male			
only females			
Units: Subjects			
Female	13	15	18
Race/Ethnicity, Customized			
Race			
Units: Subjects			
Asian	2	3	5
Black or African	0	1	0

race unknown	2	0	0
White	9	11	13
Race/Ethnicity, Customized			
Ethnicity			
Units: Subjects			
not Hispanic or Latino	6	10	16
Not reported	7	3	2
ethnicity unknown	0	2	0

Reporting group values	LEE011 + BKM120 + fulvestrant	Total	
Number of subjects	24	70	
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)	19	49	
From 65-84 years	5	21	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	56.5		
standard deviation	± 10.21	-	
Sex: Female, Male			
only females			
Units: Subjects			
Female	24	70	
Race/Ethnicity, Customized			
Race			
Units: Subjects			
Asian	10	20	
Black or African	0	1	
race unknown	3	5	
White	11	44	
Race/Ethnicity, Customized			
Ethnicity			
Units: Subjects			
not Hispanic or Latino	14	46	
Not reported	8	20	
ethnicity unknown	2	4	

Subject analysis sets

Subject analysis set title	LEE011 400mg+BKM120 30mg+Fulvestrant
Subject analysis set type	Sub-group analysis

Subject analysis set description:

LEE011 400mg+BKM120 30mg+Fulvestrant
500mg

Subject analysis set title	LEE011 400mg+BKM120 40mg+Fulvestrant
Subject analysis set type	Sub-group analysis

Subject analysis set description:

LEE011 400mg+BKM120 40mg+Fulvestrant
500mg

Subject analysis set title	LEE011 600mg+BKM120 30mg+Fulvestrant
Subject analysis set type	Sub-group analysis

Subject analysis set description:

LEE011 600mg+BKM120 30mg+Fulvestrant
500mg

Subject analysis set title	LEE011 + BYL719 200mg+ fulvestrant
Subject analysis set type	Sub-group analysis

Subject analysis set description:

LEE011 200mg+BYL719 200mg+Fulvestrant

Subject analysis set title	LEE011 400mg+BYL719 150mg+Fulvestrant
Subject analysis set type	Sub-group analysis

Subject analysis set description:

LEE011 400mg+BYL719 150mg+Fulvestrant

Subject analysis set title	LEE011 400mg+BYL719 200mg+Fulvestrant
Subject analysis set type	Sub-group analysis

Subject analysis set description:

LEE011 400mg+BYL719 200mg+Fulvestrant
500mg

Subject analysis set title	escalation cohorts
Subject analysis set type	Per protocol

Subject analysis set description:

escalation cohorts in combination arms

Reporting group values	LEE011 400mg+BKM120 30mg+Fulvestrant	LEE011 400mg+BKM120 40mg+Fulvestrant	LEE011 600mg+BKM120 30mg+Fulvestrant
Number of subjects	10	6	8
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)	8	5	6
From 65-84 years	2	1	2
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	56.5	56.5	56.5
standard deviation	± 10.21	± 10.21	± 10.21

Sex: Female, Male			
only females			
Units: Subjects			
Female	10	6	8
Race/Ethnicity, Customized			
Race			
Units: Subjects			
Asian	0	0	0
Black or African	0	0	0
race unknown	10	6	8
White	0	0	0
Race/Ethnicity, Customized			
Ethnicity			
Units: Subjects			
not Hispanic or Latino	0	0	0
Not reported	0	0	0
ethnicity unknown	10	6	8

Reporting group values	LEE011 + BYL719 200mg+ fulvestrant	LEE011 400mg+BYL719 150mg+Fulvestrant	LEE011 400mg+BYL719 200mg+Fulvestrant
Number of subjects	3	6	9
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)	1	4	6
From 65-84 years	2	2	3
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	57.5	57.5	57.5
standard deviation	± 8.81	± 8.81	± 8.81
Sex: Female, Male			
only females			
Units: Subjects			
Female	3	6	9
Race/Ethnicity, Customized			
Race			
Units: Subjects			
Asian	0	0	0
Black or African	0	0	0
race unknown	3	6	9
White	0	0	0
Race/Ethnicity, Customized			
Ethnicity			
Units: Subjects			

not Hispanic or Latino	0	0	0
Not reported	0	0	0
ethnicity unknown	3	6	9

Reporting group values	escalation cohorts		
Number of subjects	42		
Age categorical			
Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous			
Units: years			
arithmetic mean	58.3		
standard deviation	± 9.90		
Sex: Female, Male			
only females			
Units: Subjects			
Female	42		
Race/Ethnicity, Customized			
Race			
Units: Subjects			
Asian	0		
Black or African	0		
race unknown	42		
White	0		
Race/Ethnicity, Customized			
Ethnicity			
Units: Subjects			
not Hispanic or Latino	0		
Not reported	0		
ethnicity unknown	42		

End points

End points reporting groups

Reporting group title	LEE011 600 mg + fulvestrant
Reporting group description: LEE011 - 28 day cycles (3 weeks on, 1 week off), fulvestrant - 500 mg i.m. given on Day 1 and Day 15 of Cycle 1, then on Day 1 of each subsequent cycle.	
Reporting group title	LEE011 continuous 400mg cont. + fulvestrant
Reporting group description: LEE011 + fulvestrant Edit LEE011 - 28 day cycles (continuous daily dosing - dose escalating) fulvestrant - 500 mg i.m. given on Day 1 and Day 15 of Cycle 1, then on Day 1 of each subsequent cycle.	
Reporting group title	LEE011 + BYL719 + fulvestrant
Reporting group description: LEE011 - 28 day cycles (21 days followed by a 7 day break - dose escalating) BYL719 - daily (dose escalating) fulvestrant - i.m. - 500 mg given on day 1 and day 15 of Cycle 1, then on Day 1 of each subsequent cycle.	
Reporting group title	LEE011 + BKM120 + fulvestrant
Reporting group description: LEE011 - 28 day cycles (21 days followed by a 7 day break - dose escalating) BKM120 - daily (dose escalating) fulvestrant - i.m. - 500 mg given on day 1 and day 15 of Cycle 1, then on Day 1 of each subsequent cycle.	
Subject analysis set title	LEE011 400mg+BKM120 30mg+Fulvestrant
Subject analysis set type	Sub-group analysis
Subject analysis set description: LEE011 400mg+BKM120 30mg+Fulvestrant 500mg	
Subject analysis set title	LEE011 400mg+BKM120 40mg+Fulvestrant
Subject analysis set type	Sub-group analysis
Subject analysis set description: LEE011 400mg+BKM120 40mg+Fulvestrant 500mg	
Subject analysis set title	LEE011 600mg+BKM120 30mg+Fulvestrant
Subject analysis set type	Sub-group analysis
Subject analysis set description: LEE011 600mg+BKM120 30mg+Fulvestrant 500mg	
Subject analysis set title	LEE011 + BYL719 200mg+ fulvestrant
Subject analysis set type	Sub-group analysis
Subject analysis set description: LEE011 200mg+BYL719 200mg+Fulvestrant	
Subject analysis set title	LEE011 400mg+BYL719 150mg+Fulvestrant
Subject analysis set type	Sub-group analysis
Subject analysis set description: LEE011 400mg+BYL719 150mg+Fulvestrant	
Subject analysis set title	LEE011 400mg+BYL719 200mg+Fulvestrant
Subject analysis set type	Sub-group analysis
Subject analysis set description: LEE011 400mg+BYL719 200mg+Fulvestrant 500mg	
Subject analysis set title	escalation cohorts
Subject analysis set type	Per protocol
Subject analysis set description: escalation cohorts in combination arms	

Primary: Incidence of Dose limiting toxicities (DLTs) - Phase Ib only

End point title	Incidence of Dose limiting toxicities (DLTs) - Phase Ib only ^[1]
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End point description:

Dose limiting toxicities : number of participants with a dose limiting toxicity

End point type	Primary
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End point timeframe:

28 days

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: no statistic analysis was performed

End point values	LEE011 600 mg + fulvestrant	LEE011 continuous 400mg cont. + fulvestrant	LEE011 + BYL719 + fulvestrant	LEE011 + BKM120 + fulvestrant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	15	15	21
Units: participants	1	1	5	5

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration-time profiles of LEE011, BKM120, BYL719

End point title	Plasma concentration-time profiles of LEE011, BKM120, BYL719
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End point description:

To characterize the PK profiles of LEE011, BKM120, BYL719, and fulvestrant when used in combination as well as to evaluate any other clinically significant metabolites that may be identified.

End point type	Secondary
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End point timeframe:

Day 21

End point values	LEE011 600 mg + fulvestrant	LEE011 continuous 400mg cont. + fulvestrant	LEE011 + BYL719 + fulvestrant	LEE011 + BKM120 + fulvestrant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	15	18 ^[2]	24 ^[3]
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
LEE011	1840 (± 51.1)	1110 (± 50.9)	0 (± 0)	0 (± 0)
LEQ803 (LEE011 metabolite)	168 (± 66.1)	105 (± 40.1)	0 (± 0)	0 (± 0)
BYL719	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)
BKM120	0 (± 0)	0 (± 0)	0 (± 0)	0 (± 0)

Notes:

[2] - reported by specific BYL719 dose

[3] - reported by specific BKM120 dose

End point values	LEE011 400mg+BKM120 30mg+Fulvestrant	LEE011 400mg+BKM120 40mg+Fulvestrant	LEE011 600mg+BKM120 30mg+Fulvestrant	LEE011 + BYL719 200mg+ fulvestrant
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	6	8	3
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
LEE011	980 (± 40.8)	1010 (± 67.5)	2210 (± 36.0)	284 (± 42.7)
LEQ803 (LEE011 metabolite)	157 (± 46.3)	95 (± 95.3)	180 (± 3.5)	47.1 (± 84.5)
BYL719	0 (± 0)	0 (± 0)	0 (± 0)	1860 (± 14.5)
BKM120	769 (± 64.9)	771 (± 60.0)	482 (± 56.0)	0 (± 0)

End point values	LEE011 400mg+BYL719 150mg+Fulvestrant	LEE011 400mg+BYL719 200mg+Fulvestrant		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	9		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
LEE011	622 (± 33.7)	960 (± 25.4)		
LEQ803 (LEE011 metabolite)	106 (± 18.9)	107 (± 71.2)		
BYL719	1730 (± 13.7)	2130 (± 36.1)		
BKM120	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)
End point description: ORR is defined as the proportion of patients with a best overall response of complete response or partial response.	
End point type	Secondary
End point timeframe: 36 months	

End point values	LEE011 600 mg + fulvestrant	LEE011 continuous 400mg cont. + fulvestrant	LEE011 + BYL719 + fulvestrant	LEE011 + BKM120 + fulvestrant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	15	18	24
Units: participants	3	2	3	6

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) (phase I only)

End point title	Progression Free Survival (PFS) (phase I only)
End point description: PFS given as the number of participants with PFS Events during the 24 months timeframe. PFS event defined as the first documented progression or death due to any cause.	
End point type	Secondary
End point timeframe: 24 months	

End point values	LEE011 600 mg + fulvestrant	LEE011 continuous 400mg cont. + fulvestrant	LEE011 + BYL719 + fulvestrant	LEE011 + BKM120 + fulvestrant
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	15	18	24
Units: participants	11	9	12	17

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

up to 24 months

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	LEE011 600mg+Fulvestrant
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Reporting group description:

LEE011 600mg+Fulvestrant

Reporting group title	LEE011 400mg (cont.)+@Fulvestrant
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Reporting group description:

LEE011 400mg (cont.)+@Fulvestrant

Reporting group title	LEE011 200mg+@BYL719 200mg+@Fulvestrant
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Reporting group description:

LEE011 200mg+@BYL719 200mg+@Fulvestrant

Reporting group title	LEE011 400mg+@BYL719 150mg+@Fulvestrant
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Reporting group description:

LEE011 400mg+@BYL719 150mg+@Fulvestrant

Reporting group title	LEE011 400mg+@BYL719 200mg+@Fulvestrant
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Reporting group description:

LEE011 400mg+@BYL719 200mg+@Fulvestrant

Reporting group title	LEE011 400mg+@BKM120 30mg+@Fulvestrant
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Reporting group description:

LEE011 400mg+@BKM120 30mg+@Fulvestrant

Reporting group title	LEE011 400mg+@BKM120 40mg+@Fulvestrant
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Reporting group description:

LEE011 400mg+@BKM120 40mg+@Fulvestrant

Reporting group title	LEE011 600mg+@BKM120 30mg+@Fulvestrant
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Reporting group description:

LEE011 600mg+@BKM120 30mg+@Fulvestrant

Reporting group title	All subjects@(doublets)@LEE+ Fulvestrant
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Reporting group description:

All subjects@(doublets)@LEE+ Fulvestrant

Reporting group title	All subjects@(triplets)@LEE + BYL + Fulvestrant
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Reporting group description:

All subjects@(triplets)@LEE + BYL + Fulvestrant

Reporting group title	All subjects@(triplets)@LEE + BKM + Fulvestrant
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Reporting group description:

All subjects@(triplets)@LEE + BKM + Fulvestrant

Reporting group title	All@subjects
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Reporting group description:

All@subjects

Serious adverse events	LEE011 600mg+Fulvestrant	LEE011 400mg (cont.)+@Fulvestrant	LEE011 200mg+@BYL719 200mg+@Fulvestrant
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 13 (61.54%)	3 / 15 (20.00%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (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
Tumour pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (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
Pyrexia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (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

Interstitial lung disease			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (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
Pleural effusion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (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
Mental status changes			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	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
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (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			
Overdose			

subjects affected / exposed	2 / 13 (15.38%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	2 / 13 (15.38%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	2 / 13 (15.38%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (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	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			

subjects affected / exposed	2 / 13 (15.38%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (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
Hepatic function abnormal			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (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
Rash maculo-papular			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (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
Pain in extremity			

subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (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
Pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	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
Pyelonephritis acute			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (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
Sepsis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (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
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (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
Varicella			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	LEE011 400mg+@BYL719 150mg+@Fulvestrant	LEE011 400mg+@BYL719 200mg+@Fulvestrant	LEE011 400mg+@BKM120 30mg+@Fulvestrant
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	3 / 9 (33.33%)	3 / 10 (30.00%)
number of deaths (all causes)	0	0	0

number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 10 (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
Tumour pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
Interstitial lung disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
Mental status changes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 10 (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
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Drug-induced liver injury			

subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (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			
Bronchitis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (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

Serious adverse events	LEE011 400mg+@BKM120 40mg+@Fulvestrant	LEE011 600mg+@BKM120 30mg+@Fulvestrant	All subjects@ (doublets) @LEE+ Fulvestrant
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)	4 / 8 (50.00%)	11 / 28 (39.29%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (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
Tumour pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (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 / 8 (25.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 1
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%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (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
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (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

Pulmonary embolism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (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			
Overdose			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	3 / 28 (10.71%)
occurrences causally related to treatment / all	0 / 0	1 / 1	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (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
Hepatic function abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (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
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
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 in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			

subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 28 (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
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (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
Urinary tract infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 28 (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
Varicella			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	All subjects@(triplets)@LEE + BYL +	All subjects@(triplets)@LEE + BKM +	All@subjects
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 18 (33.33%)	9 / 24 (37.50%)	26 / 70 (37.14%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 18 (0.00%)	2 / 24 (8.33%)	3 / 70 (4.29%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Mental status changes			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 18 (5.56%)	1 / 24 (4.17%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	1 / 1	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	3 / 70 (4.29%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			

subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	4 / 70 (5.71%)
occurrences causally related to treatment / all	0 / 0	1 / 1	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	3 / 70 (4.29%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
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 in extremity			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 24 (4.17%)	3 / 70 (4.29%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	0 / 18 (0.00%)	2 / 24 (8.33%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	LEE011 600mg+Fulvestrant	LEE011 400mg (cont.)+@Fulvestrant	LEE011 200mg+@BYL719 200mg+@Fulvestrant
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 13 (100.00%)	15 / 15 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 13 (7.69%)	2 / 15 (13.33%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Hypotension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral coldness			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 13 (7.69%)	3 / 15 (20.00%)	0 / 3 (0.00%)
occurrences (all)	1	6	0
Catheter site dermatitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Catheter site pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter site pruritus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 13 (0.00%)	2 / 15 (13.33%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Fatigue			
subjects affected / exposed	9 / 13 (69.23%)	8 / 15 (53.33%)	1 / 3 (33.33%)
occurrences (all)	11	8	1
Gait disturbance			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Impaired healing			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Injection site pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Mucosal inflammation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Oedema peripheral subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	2 / 15 (13.33%) 2	0 / 3 (0.00%) 0
Pain subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 15 (0.00%) 0	0 / 3 (0.00%) 0
Peripheral swelling subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 15 (0.00%) 0	0 / 3 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	3 / 13 (23.08%) 3	2 / 15 (13.33%) 3	0 / 3 (0.00%) 0
Temperature intolerance subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 15 (6.67%) 2	0 / 3 (0.00%) 0
Immune system disorders Contrast media reaction subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 15 (0.00%) 0	0 / 3 (0.00%) 0
Drug hypersensitivity subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 15 (0.00%) 0	0 / 3 (0.00%) 0
Reproductive system and breast disorders Breast pain subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 15 (0.00%) 0	0 / 3 (0.00%) 0
Vaginal haemorrhage subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 15 (0.00%) 0	0 / 3 (0.00%) 0
Vulvovaginal dryness subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 15 (0.00%) 0	0 / 3 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Chronic obstructive pulmonary disease			

subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	5 / 13 (38.46%)	0 / 15 (0.00%)	1 / 3 (33.33%)
occurrences (all)	5	0	1
Dysphonia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dyspnoea exertional			
subjects affected / exposed	2 / 13 (15.38%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypoxia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Interstitial lung disease			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pneumonitis			
subjects affected / exposed	2 / 13 (15.38%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Productive cough			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Respiratory tract congestion			

subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Sinus congestion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 13 (15.38%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Confusional state			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Emotional distress			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Mood altered			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mood swings			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 13 (30.77%)	4 / 15 (26.67%)	2 / 3 (66.67%)
occurrences (all)	4	5	2
Amylase increased			
subjects affected / exposed	2 / 13 (15.38%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 13 (38.46%)	4 / 15 (26.67%)	1 / 3 (33.33%)
occurrences (all)	5	6	1
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 13 (15.38%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Blood bilirubin increased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Blood calcium decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood chloride decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood chloride increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	2 / 13 (15.38%)	2 / 15 (13.33%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Blood glucose increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood potassium decreased			

subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	2 / 13 (15.38%)	2 / 15 (13.33%)	0 / 3 (0.00%)
occurrences (all)	3	3	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Haematocrit decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Heart rate increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	2 / 13 (15.38%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Monocyte count increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	2 / 13 (15.38%)	2 / 15 (13.33%)	1 / 3 (33.33%)
occurrences (all)	4	3	2
Platelet count decreased			
subjects affected / exposed	3 / 13 (23.08%)	0 / 15 (0.00%)	1 / 3 (33.33%)
occurrences (all)	6	0	1

Protein total decreased subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 15 (0.00%) 0	0 / 3 (0.00%) 0
Transaminases increased subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 15 (6.67%) 1	0 / 3 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 15 (0.00%) 0	0 / 3 (0.00%) 0
Weight increased subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 15 (6.67%) 1	0 / 3 (0.00%) 0
White blood cell count decreased subjects affected / exposed occurrences (all)	4 / 13 (30.77%) 4	2 / 15 (13.33%) 2	1 / 3 (33.33%) 1
Injury, poisoning and procedural complications			
Foot fracture subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 15 (0.00%) 0	0 / 3 (0.00%) 0
Infusion related reaction subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 15 (6.67%) 1	0 / 3 (0.00%) 0
Overdose subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 15 (0.00%) 0	0 / 3 (0.00%) 0
Radiation pneumonitis subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 15 (0.00%) 0	0 / 3 (0.00%) 0
Wound complication subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 15 (0.00%) 0	0 / 3 (0.00%) 0
Cardiac disorders			
Atrioventricular block first degree subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 15 (0.00%) 0	0 / 3 (0.00%) 0
Palpitations			

subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pericardial effusion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Supraventricular tachycardia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	2 / 13 (15.38%)	1 / 15 (6.67%)	1 / 3 (33.33%)
occurrences (all)	2	1	2
Dysgeusia			
subjects affected / exposed	2 / 13 (15.38%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Headache			
subjects affected / exposed	1 / 13 (7.69%)	3 / 15 (20.00%)	1 / 3 (33.33%)
occurrences (all)	1	3	2
Hyperaesthesia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Migraine with aura			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Neuralgia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Neuropathy peripheral			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Parosmia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 13 (0.00%)	2 / 15 (13.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Visual field defect			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 13 (46.15%)	2 / 15 (13.33%)	0 / 3 (0.00%)
occurrences (all)	10	2	0
Anaemia macrocytic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Increased tendency to bruise			

subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	1 / 13 (7.69%)	2 / 15 (13.33%)	1 / 3 (33.33%)
occurrences (all)	1	2	1
Lymphopenia			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Neutropenia			
subjects affected / exposed	10 / 13 (76.92%)	10 / 15 (66.67%)	0 / 3 (0.00%)
occurrences (all)	11	19	0
Thrombocytopenia			
subjects affected / exposed	3 / 13 (23.08%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	5	0	0
Eye disorders			
Asthenopia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cataract			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Corneal deposits			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Eye swelling			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ocular hyperaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Strabismus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Abdominal pain			
subjects affected / exposed	1 / 13 (7.69%)	5 / 15 (33.33%)	2 / 3 (66.67%)
occurrences (all)	1	8	2
Abdominal pain upper			
subjects affected / exposed	2 / 13 (15.38%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Aphthous ulcer			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Bowel movement irregularity			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 13 (7.69%)	4 / 15 (26.67%)	2 / 3 (66.67%)
occurrences (all)	1	6	3
Diarrhoea			
subjects affected / exposed	4 / 13 (30.77%)	4 / 15 (26.67%)	3 / 3 (100.00%)
occurrences (all)	6	4	4
Dry mouth			

subjects affected / exposed	0 / 13 (0.00%)	2 / 15 (13.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Dyspepsia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Dysphagia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Epigastric discomfort			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eructation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Faeces soft			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Haemorrhoids			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Mouth ulceration			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	7 / 13 (53.85%)	9 / 15 (60.00%)	2 / 3 (66.67%)
occurrences (all)	8	9	2
Odynophagia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oesophagitis			

subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	2 / 13 (15.38%)	1 / 15 (6.67%)	1 / 3 (33.33%)
occurrences (all)	2	1	1
Stomatitis			
subjects affected / exposed	0 / 13 (0.00%)	3 / 15 (20.00%)	1 / 3 (33.33%)
occurrences (all)	0	4	1
Vomiting			
subjects affected / exposed	5 / 13 (38.46%)	3 / 15 (20.00%)	2 / 3 (66.67%)
occurrences (all)	12	6	2
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Dermatitis allergic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Madarosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			

subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	4 / 13 (30.77%)	4 / 15 (26.67%)	0 / 3 (0.00%)
occurrences (all)	5	10	0
Rash			
subjects affected / exposed	1 / 13 (7.69%)	2 / 15 (13.33%)	1 / 3 (33.33%)
occurrences (all)	4	2	1
Rash maculo-papular			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin discolouration			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin hypopigmentation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vitiligo			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Chromaturia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Nocturia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Strangury			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Urinary hesitation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 13 (15.38%)	4 / 15 (26.67%)	0 / 3 (0.00%)
occurrences (all)	2	9	0
Back pain			
subjects affected / exposed	1 / 13 (7.69%)	3 / 15 (20.00%)	1 / 3 (33.33%)
occurrences (all)	1	6	1
Bone pain			
subjects affected / exposed	1 / 13 (7.69%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Joint swelling			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			

subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Muscular weakness			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	2 / 13 (15.38%)	2 / 15 (13.33%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Myalgia			
subjects affected / exposed	1 / 13 (7.69%)	2 / 15 (13.33%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Neck pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Osteonecrosis of jaw			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 13 (7.69%)	3 / 15 (20.00%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Pain in jaw			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Scoliosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Catheter site infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0

Ear infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear infection fungal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Escherichia infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatitis B			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Herpes simplex			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Herpes virus infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 13 (0.00%)	2 / 15 (13.33%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Mastitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 13 (0.00%)	2 / 15 (13.33%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Oral candidiasis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tinea infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 13 (15.38%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 13 (46.15%)	2 / 15 (13.33%)	1 / 3 (33.33%)
occurrences (all)	7	2	1
Dehydration			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	2 / 13 (15.38%)	0 / 15 (0.00%)	2 / 3 (66.67%)
occurrences (all)	2	0	3
Hyperkalaemia			

subjects affected / exposed	0 / 13 (0.00%)	1 / 15 (6.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypermagnesaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypernatraemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	2 / 13 (15.38%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypomagnesaemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	2 / 13 (15.38%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 15 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	LEE011 400mg+@BYL719 150mg+@Fulvestrant	LEE011 400mg+@BYL719 200mg+@Fulvestrant	LEE011 400mg+@BKM120 30mg+@Fulvestrant
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	9 / 9 (100.00%)	10 / 10 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Malignant melanoma subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Vascular disorders			
Hot flush subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Hypotension subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Peripheral coldness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
General disorders and administration site conditions			
Asthenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 2	1 / 10 (10.00%) 2
Catheter site dermatitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Catheter site pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Catheter site pruritus subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Chest discomfort subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 9 (22.22%) 2	0 / 10 (0.00%) 0
Chills subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	1 / 10 (10.00%) 2
Fatigue subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 3	6 / 9 (66.67%) 7	6 / 10 (60.00%) 8
Gait disturbance			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	3
Impaired healing			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Peripheral swelling			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	2	2	3
Temperature intolerance			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			

Contrast media reaction subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Drug hypersensitivity subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Reproductive system and breast disorders			
Breast pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Vaginal haemorrhage subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Vulvovaginal dryness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Cough subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	2 / 9 (22.22%) 2	1 / 10 (10.00%) 1
Dysphonia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	2 / 10 (20.00%) 4
Dyspnoea exertional subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Hypoxia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1

Interstitial lung disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pneumonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Respiratory tract congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Sinus congestion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	4
Confusional state			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Emotional distress			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	1 / 6 (16.67%)	3 / 9 (33.33%)	0 / 10 (0.00%)
occurrences (all)	1	3	0
Mood altered			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Mood swings			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	5 / 6 (83.33%)	1 / 9 (11.11%)	5 / 10 (50.00%)
occurrences (all)	6	1	6
Amylase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 6 (83.33%)	1 / 9 (11.11%)	5 / 10 (50.00%)
occurrences (all)	6	1	6
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			

subjects affected / exposed	2 / 6 (33.33%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	4	0	0
Blood calcium decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Blood chloride decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Blood chloride increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	2 / 6 (33.33%)	1 / 9 (11.11%)	3 / 10 (30.00%)
occurrences (all)	5	1	3
Blood glucose increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Blood sodium decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	1	1	2
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Haematocrit decreased			

subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Haemoglobin decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Heart rate increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Monocyte count increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Neutrophil count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	3
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Protein total decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Transaminases increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	2 / 6 (33.33%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	2	1	1
Weight increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	2 / 10 (20.00%) 2
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Infusion related reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Overdose			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Radiation pneumonitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Wound complication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Sinus bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Supraventricular tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tachycardia			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 2
Nervous system disorders			
Ataxia			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Dizziness			
subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 4	1 / 9 (11.11%) 1	1 / 10 (10.00%) 2
Dysgeusia			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Headache			
subjects affected / exposed occurrences (all)	4 / 6 (66.67%) 6	0 / 9 (0.00%) 0	1 / 10 (10.00%) 2
Hyperaesthesia			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Hypoaesthesia			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Migraine with aura			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Neuralgia			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Neuropathy peripheral			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Paraesthesia			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Parosmia			
subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1

Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Somnolence subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Syncope subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Tremor subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Visual field defect subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	2 / 9 (22.22%) 3	0 / 10 (0.00%) 0
Anaemia macrocytic subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Increased tendency to bruise subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Leukopenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Lymphopenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Neutropenia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	7 / 9 (77.78%) 12	8 / 10 (80.00%) 15
Thrombocytopenia			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	5 / 9 (55.56%) 7	2 / 10 (20.00%) 2
Eye disorders			
Asthenopia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cataract			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Corneal deposits			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Eye swelling			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Lacrimation increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Strabismus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Aphthous ulcer			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Ascites			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Bowel movement irregularity			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	2 / 6 (33.33%)	1 / 9 (11.11%)	2 / 10 (20.00%)
occurrences (all)	2	1	2
Diarrhoea			
subjects affected / exposed	2 / 6 (33.33%)	3 / 9 (33.33%)	4 / 10 (40.00%)
occurrences (all)	2	9	7
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	1 / 6 (16.67%)	3 / 9 (33.33%)	1 / 10 (10.00%)
occurrences (all)	1	4	1
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Epigastric discomfort			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Eructation			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Faeces soft			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Haemorrhoids			
subjects affected / exposed	2 / 6 (33.33%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Mouth ulceration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	3 / 6 (50.00%)	7 / 9 (77.78%)	6 / 10 (60.00%)
occurrences (all)	4	10	9
Odynophagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oesophagitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Oral pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	5 / 9 (55.56%)	2 / 10 (20.00%)
occurrences (all)	0	7	4
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	2 / 9 (22.22%)	4 / 10 (40.00%)
occurrences (all)	2	2	5
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Dermatitis allergic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	3 / 10 (30.00%)
occurrences (all)	0	0	3
Eczema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Madarosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nail disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	2 / 10 (20.00%)
occurrences (all)	1	4	2
Rash			
subjects affected / exposed	1 / 6 (16.67%)	6 / 9 (66.67%)	5 / 10 (50.00%)
occurrences (all)	1	11	6
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	3 / 10 (30.00%)
occurrences (all)	0	1	4
Rash pruritic			

subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Skin discolouration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Skin exfoliation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Skin hypopigmentation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Skin irritation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Vitiligo			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Chromaturia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Dysuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nocturia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0

Strangury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urinary hesitation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	2 / 10 (20.00%)
occurrences (all)	2	2	3
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	3 / 10 (30.00%)
occurrences (all)	0	0	3
Muscular weakness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Myalgia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Osteonecrosis of jaw			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pain in jaw			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Scoliosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Catheter site infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Ear infection fungal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Escherichia infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

Hepatitis B			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Herpes simplex			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Herpes virus infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Mastitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Tinea infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)	2 / 9 (22.22%)	1 / 10 (10.00%)
occurrences (all)	1	2	1

Urinary tract infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 2
Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	4 / 9 (44.44%) 4	3 / 10 (30.00%) 3
Dehydration subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	2 / 10 (20.00%) 2
Hypercalcaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Hypercholesterolaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Hyperglycaemia subjects affected / exposed occurrences (all)	5 / 6 (83.33%) 8	5 / 9 (55.56%) 7	4 / 10 (40.00%) 8
Hyperkalaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Hypermagnesaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Hypernatraemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Hypoalbuminaemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Hypocalcaemia			

subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Hypomagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hyponatraemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Hypophosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	LEE011 400mg+@BKM120 40mg+@Fulvestrant	LEE011 600mg+@BKM120 30mg+@Fulvestrant	All subjects@(doublets) @LEE+ Fulvestrant
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	8 / 8 (100.00%)	28 / 28 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	3 / 28 (10.71%)
occurrences (all)	0	0	3
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Peripheral coldness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	4 / 28 (14.29%)
occurrences (all)	0	4	7
Catheter site dermatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Catheter site pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Catheter site pruritus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Chest discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	3
Fatigue			
subjects affected / exposed	4 / 6 (66.67%)	4 / 8 (50.00%)	17 / 28 (60.71%)
occurrences (all)	4	7	19
Gait disturbance			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Impaired healing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	1	0	1
Injection site pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Malaise			

subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	1	0	2
Mucosal inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	2 / 28 (7.14%)
occurrences (all)	0	1	2
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 8 (25.00%)	5 / 28 (17.86%)
occurrences (all)	1	2	6
Temperature intolerance			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	2
Immune system disorders			
Contrast media reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Drug hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Vulvovaginal dryness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	5 / 28 (17.86%)
occurrences (all)	1	0	5
Dysphonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	1 / 28 (3.57%)
occurrences (all)	0	3	1
Dyspnoea exertional			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	1	0	2
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Interstitial lung disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Paranasal sinus hypersecretion			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Pneumonitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	2 / 28 (7.14%)
occurrences (all)	0	1	2
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Respiratory tract congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Sinus congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	3 / 28 (10.71%)
occurrences (all)	0	2	3
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Depressed mood			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	1	0	3
Emotional distress			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0

Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	1 / 28 (3.57%)
occurrences (all)	0	2	1
Mood altered			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	0 / 28 (0.00%)
occurrences (all)	0	3	0
Mood swings			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 6 (50.00%)	3 / 8 (37.50%)	8 / 28 (28.57%)
occurrences (all)	5	3	9
Amylase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	2 / 28 (7.14%)
occurrences (all)	0	1	2
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 6 (66.67%)	5 / 8 (62.50%)	9 / 28 (32.14%)
occurrences (all)	6	6	11
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	3 / 28 (10.71%)
occurrences (all)	0	2	3
Blood bilirubin increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	1	0	3
Blood calcium decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Blood chloride decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Blood chloride increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			

subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	4 / 28 (14.29%)
occurrences (all)	1	0	4
Blood glucose increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	1 / 28 (3.57%)
occurrences (all)	0	1	1
Blood potassium decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	4 / 28 (14.29%)
occurrences (all)	0	1	6
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	1	0	1
Haematocrit decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Heart rate increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Lipase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			

subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	2 / 28 (7.14%)
occurrences (all)	1	3	3
Monocyte count increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	4 / 28 (14.29%)
occurrences (all)	2	1	7
Platelet count decreased			
subjects affected / exposed	1 / 6 (16.67%)	2 / 8 (25.00%)	3 / 28 (10.71%)
occurrences (all)	1	7	6
Protein total decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	1 / 28 (3.57%)
occurrences (all)	0	2	1
Weight decreased			
subjects affected / exposed	3 / 6 (50.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	3	1	0
Weight increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
White blood cell count decreased			
subjects affected / exposed	1 / 6 (16.67%)	2 / 8 (25.00%)	6 / 28 (21.43%)
occurrences (all)	1	5	6
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Overdose			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Radiation pneumonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Wound complication			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Atrioventricular block first degree			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	1	0	1
Pericardial effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Supraventricular tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	3 / 28 (10.71%)
occurrences (all)	0	2	3
Dysgeusia			

subjects affected / exposed	2 / 6 (33.33%)	3 / 8 (37.50%)	2 / 28 (7.14%)
occurrences (all)	2	5	2
Headache			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	4 / 28 (14.29%)
occurrences (all)	0	2	4
Hyperaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	1	1	0
Migraine with aura			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Neuralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Neuropathy peripheral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Parosmia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Tremor			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Visual field defect			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 8 (25.00%)	8 / 28 (28.57%)
occurrences (all)	1	2	12
Anaemia macrocytic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Increased tendency to bruise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	3 / 28 (10.71%)
occurrences (all)	0	2	3
Lymphopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Neutropenia			
subjects affected / exposed	4 / 6 (66.67%)	5 / 8 (62.50%)	20 / 28 (71.43%)
occurrences (all)	6	9	30
Thrombocytopenia			
subjects affected / exposed	2 / 6 (33.33%)	2 / 8 (25.00%)	3 / 28 (10.71%)
occurrences (all)	2	4	5
Eye disorders			
Asthenopia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Cataract			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Corneal deposits			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Dry eye			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Eye swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	1	0	1
Ocular hyperaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Strabismus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	6 / 28 (21.43%)
occurrences (all)	1	0	9
Abdominal pain upper			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	1	0	3
Aphthous ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0

Ascites			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	1	0	1
Bowel movement irregularity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	5 / 28 (17.86%)
occurrences (all)	1	3	7
Diarrhoea			
subjects affected / exposed	2 / 6 (33.33%)	4 / 8 (50.00%)	8 / 28 (28.57%)
occurrences (all)	4	5	10
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Dyspepsia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 8 (12.50%)	1 / 28 (3.57%)
occurrences (all)	2	1	1
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Epigastric discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Eructation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	1	0	1
Faeces soft			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 6 (33.33%)	1 / 8 (12.50%)	1 / 28 (3.57%)
occurrences (all)	2	1	2

Haemorrhoids			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Mouth ulceration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	4 / 6 (66.67%)	7 / 8 (87.50%)	16 / 28 (57.14%)
occurrences (all)	4	9	17
Odynophagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Oesophagitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Oral pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	3 / 28 (10.71%)
occurrences (all)	0	0	3
Stomatitis			
subjects affected / exposed	1 / 6 (16.67%)	2 / 8 (25.00%)	3 / 28 (10.71%)
occurrences (all)	1	2	4
Vomiting			
subjects affected / exposed	2 / 6 (33.33%)	2 / 8 (25.00%)	8 / 28 (28.57%)
occurrences (all)	2	2	18
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	1	0	2
Dermatitis allergic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	2 / 6 (33.33%)	1 / 8 (12.50%)	1 / 28 (3.57%)
occurrences (all)	2	1	1
Eczema			

subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	1	0	1
Madarosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Nail disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	3 / 6 (50.00%)	3 / 8 (37.50%)	8 / 28 (28.57%)
occurrences (all)	4	4	15
Rash			
subjects affected / exposed	1 / 6 (16.67%)	4 / 8 (50.00%)	3 / 28 (10.71%)
occurrences (all)	2	9	6
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Rash pruritic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Skin discolouration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Skin hypopigmentation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0

Skin irritation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Vitiligo			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	2
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Chromaturia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	3
Nocturia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Strangury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Urinary hesitation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 8 (25.00%)	6 / 28 (21.43%)
occurrences (all)	2	2	11
Back pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	4 / 28 (14.29%)
occurrences (all)	1	1	7
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Joint swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	1 / 28 (3.57%)
occurrences (all)	0	1	1
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	4 / 28 (14.29%)
occurrences (all)	0	0	4
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	3 / 28 (10.71%)
occurrences (all)	0	1	3
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Osteonecrosis of jaw			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	4 / 28 (14.29%)
occurrences (all)	0	1	4

Pain in jaw			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Scoliosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Infections and infestations			
Catheter site infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	1 / 28 (3.57%)
occurrences (all)	0	1	2
Ear infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Ear infection fungal			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Escherichia infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Escherichia urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Hepatitis B			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Herpes simplex			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Herpes virus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Influenza			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	3
Mastitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	1	0	3
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Tinea infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	3 / 28 (10.71%)
occurrences (all)	0	0	3
Urinary tract infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 6 (50.00%)	5 / 8 (62.50%)	8 / 28 (28.57%)
occurrences (all)	3	7	9

Dehydration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Hypercholesterolaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 6 (16.67%)	4 / 8 (50.00%)	2 / 28 (7.14%)
occurrences (all)	1	6	2
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Hypermagnesaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Hypernatraemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Hypocalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 8 (0.00%)	1 / 28 (3.57%)
occurrences (all)	2	0	1
Hypomagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	1 / 28 (3.57%)
occurrences (all)	0	1	1

Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Hypophosphataemia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 8 (25.00%)	0 / 28 (0.00%)
occurrences (all)	1	2	0

Non-serious adverse events	All subjects@(triplets) @LEE + BYL +	All subjects@(triplets) LEE + BKM +	All@subjects
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 18 (100.00%)	24 / 24 (100.00%)	70 / 70 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	4 / 70 (5.71%)
occurrences (all)	1	0	4
Hypotension			
subjects affected / exposed	0 / 18 (0.00%)	2 / 24 (8.33%)	2 / 70 (2.86%)
occurrences (all)	0	2	2
Peripheral coldness			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 18 (5.56%)	2 / 24 (8.33%)	7 / 70 (10.00%)
occurrences (all)	2	6	15
Catheter site dermatitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Catheter site pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Catheter site pruritus			

subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Chest discomfort			
subjects affected / exposed	2 / 18 (11.11%)	0 / 24 (0.00%)	2 / 70 (2.86%)
occurrences (all)	2	0	2
Chills			
subjects affected / exposed	1 / 18 (5.56%)	1 / 24 (4.17%)	4 / 70 (5.71%)
occurrences (all)	1	2	6
Fatigue			
subjects affected / exposed	10 / 18 (55.56%)	14 / 24 (58.33%)	41 / 70 (58.57%)
occurrences (all)	11	19	49
Gait disturbance			
subjects affected / exposed	0 / 18 (0.00%)	2 / 24 (8.33%)	2 / 70 (2.86%)
occurrences (all)	0	3	3
Impaired healing			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Influenza like illness			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	2 / 70 (2.86%)
occurrences (all)	0	1	2
Injection site pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	2 / 70 (2.86%)
occurrences (all)	0	2	3
Malaise			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	3 / 70 (4.29%)
occurrences (all)	0	1	3
Mucosal inflammation			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	2 / 70 (2.86%)
occurrences (all)	0	1	2
Oedema peripheral			
subjects affected / exposed	2 / 18 (11.11%)	2 / 24 (8.33%)	6 / 70 (8.57%)
occurrences (all)	2	2	6
Pain			

subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	1 / 70 (1.43%) 1
Peripheral swelling subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	1 / 24 (4.17%) 1	2 / 70 (2.86%) 2
Pyrexia subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 4	4 / 24 (16.67%) 6	12 / 70 (17.14%) 16
Temperature intolerance subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 24 (0.00%) 0	2 / 70 (2.86%) 3
Immune system disorders Contrast media reaction subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	1 / 70 (1.43%) 1
Drug hypersensitivity subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	1 / 70 (1.43%) 1
Reproductive system and breast disorders Breast pain subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
Vaginal haemorrhage subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
Vulvovaginal dryness subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	1 / 70 (1.43%) 1
Respiratory, thoracic and mediastinal disorders Chronic obstructive pulmonary disease subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	1 / 70 (1.43%) 1
Cough subjects affected / exposed occurrences (all)	4 / 18 (22.22%) 4	2 / 24 (8.33%) 2	11 / 70 (15.71%) 11

Dysphonia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Dyspnoea			
subjects affected / exposed	0 / 18 (0.00%)	4 / 24 (16.67%)	5 / 70 (7.14%)
occurrences (all)	0	7	8
Dyspnoea exertional			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	3 / 70 (4.29%)
occurrences (all)	0	1	3
Hypoxia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Interstitial lung disease			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Nasal congestion			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	2 / 70 (2.86%)
occurrences (all)	0	1	2
Oropharyngeal pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	3 / 70 (4.29%)
occurrences (all)	1	0	3
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Pneumonitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	3 / 70 (4.29%)
occurrences (all)	0	1	3
Productive cough			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	2 / 70 (2.86%)
occurrences (all)	1	0	2
Respiratory tract congestion			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	2 / 70 (2.86%)
occurrences (all)	0	2	3
Rhinorrhoea			
subjects affected / exposed	2 / 18 (11.11%)	0 / 24 (0.00%)	4 / 70 (5.71%)
occurrences (all)	2	0	4

Sinus congestion subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
Wheezing subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	1 / 70 (1.43%) 1
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	4 / 24 (16.67%) 6	8 / 70 (11.43%) 10
Confusional state subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	1 / 70 (1.43%) 1
Depressed mood subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	1 / 70 (1.43%) 1
Depression subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	2 / 24 (8.33%) 3	4 / 70 (5.71%) 6
Emotional distress subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	1 / 70 (1.43%) 1
Insomnia subjects affected / exposed occurrences (all)	5 / 18 (27.78%) 5	2 / 24 (8.33%) 2	8 / 70 (11.43%) 8
Mood altered subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	3 / 24 (12.50%) 4	3 / 70 (4.29%) 4
Mood swings subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	8 / 18 (44.44%) 9	11 / 24 (45.83%) 14	27 / 70 (38.57%) 32
Amylase increased			

subjects affected / exposed	0 / 18 (0.00%)	2 / 24 (8.33%)	4 / 70 (5.71%)
occurrences (all)	0	2	4
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 18 (38.89%)	14 / 24 (58.33%)	30 / 70 (42.86%)
occurrences (all)	8	18	37
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 18 (5.56%)	2 / 24 (8.33%)	6 / 70 (8.57%)
occurrences (all)	1	2	6
Blood bilirubin increased			
subjects affected / exposed	2 / 18 (11.11%)	1 / 24 (4.17%)	5 / 70 (7.14%)
occurrences (all)	4	1	8
Blood calcium decreased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Blood chloride decreased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Blood chloride increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Blood creatinine increased			
subjects affected / exposed	3 / 18 (16.67%)	4 / 24 (16.67%)	11 / 70 (15.71%)
occurrences (all)	6	4	14
Blood glucose increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	2 / 70 (2.86%)
occurrences (all)	0	1	2
Blood potassium decreased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Blood sodium decreased			

subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Electrocardiogram QT prolonged			
subjects affected / exposed	2 / 18 (11.11%)	2 / 24 (8.33%)	8 / 70 (11.43%)
occurrences (all)	2	3	11
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 18 (5.56%)	1 / 24 (4.17%)	3 / 70 (4.29%)
occurrences (all)	1	1	3
Haematocrit decreased			
subjects affected / exposed	1 / 18 (5.56%)	1 / 24 (4.17%)	2 / 70 (2.86%)
occurrences (all)	1	1	2
Haemoglobin decreased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Heart rate increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Lipase increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 18 (0.00%)	3 / 24 (12.50%)	5 / 70 (7.14%)
occurrences (all)	0	5	8
Monocyte count increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Neutrophil count decreased			
subjects affected / exposed	1 / 18 (5.56%)	4 / 24 (16.67%)	9 / 70 (12.86%)
occurrences (all)	2	6	15
Platelet count decreased			
subjects affected / exposed	1 / 18 (5.56%)	3 / 24 (12.50%)	7 / 70 (10.00%)
occurrences (all)	1	8	15
Protein total decreased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1

Transaminases increased subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	3 / 24 (12.50%) 3	4 / 70 (5.71%) 4
Weight decreased subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 3	5 / 24 (20.83%) 5	8 / 70 (11.43%) 8
Weight increased subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
White blood cell count decreased subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	5 / 24 (20.83%) 8	13 / 70 (18.57%) 16
Injury, poisoning and procedural complications			
Foot fracture subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
Infusion related reaction subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
Overdose subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	1 / 24 (4.17%) 1	3 / 70 (4.29%) 3
Radiation pneumonitis subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
Wound complication subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	1 / 70 (1.43%) 1
Cardiac disorders			
Atrioventricular block first degree subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
Palpitations subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	2 / 70 (2.86%) 2
Pericardial effusion			

subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Sinus bradycardia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Supraventricular tachycardia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Tachycardia			
subjects affected / exposed	0 / 18 (0.00%)	2 / 24 (8.33%)	2 / 70 (2.86%)
occurrences (all)	0	3	3
Nervous system disorders			
Ataxia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Dizziness			
subjects affected / exposed	4 / 18 (22.22%)	2 / 24 (8.33%)	9 / 70 (12.86%)
occurrences (all)	7	4	14
Dysgeusia			
subjects affected / exposed	0 / 18 (0.00%)	5 / 24 (20.83%)	7 / 70 (10.00%)
occurrences (all)	0	7	9
Headache			
subjects affected / exposed	5 / 18 (27.78%)	3 / 24 (12.50%)	12 / 70 (17.14%)
occurrences (all)	8	4	16
Hyperaesthesia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	0 / 18 (0.00%)	2 / 24 (8.33%)	2 / 70 (2.86%)
occurrences (all)	0	2	2
Migraine with aura			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Neuralgia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	2 / 70 (2.86%)
occurrences (all)	0	1	2

Neuropathy peripheral subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 24 (0.00%) 0	2 / 70 (2.86%) 2
Paraesthesia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
Parosmia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	1 / 70 (1.43%) 1
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
Somnolence subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	1 / 70 (1.43%) 1
Syncope subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	1 / 24 (4.17%) 1	2 / 70 (2.86%) 2
Tremor subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 24 (0.00%) 0	2 / 70 (2.86%) 2
Visual field defect subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 4	3 / 24 (12.50%) 3	14 / 70 (20.00%) 19
Anaemia macrocytic subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	1 / 70 (1.43%) 1
Increased tendency to bruise subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
Leukopenia			

subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	2 / 24 (8.33%) 3	6 / 70 (8.57%) 7
Lymphopenia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 24 (0.00%) 0	2 / 70 (2.86%) 2
Neutropenia subjects affected / exposed occurrences (all)	8 / 18 (44.44%) 13	17 / 24 (70.83%) 30	45 / 70 (64.29%) 73
Thrombocytopenia subjects affected / exposed occurrences (all)	5 / 18 (27.78%) 7	6 / 24 (25.00%) 8	14 / 70 (20.00%) 20
Eye disorders			
Asthenopia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	1 / 70 (1.43%) 1
Cataract subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	1 / 70 (1.43%) 1
Corneal deposits subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
Dry eye subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 2	3 / 70 (4.29%) 4
Eye swelling subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
Lacrimation increased subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	2 / 70 (2.86%) 2
Ocular hyperaemia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	1 / 70 (1.43%) 1
Strabismus subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	1 / 70 (1.43%) 1

Vision blurred subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 24 (0.00%) 0	2 / 70 (2.86%) 2
Gastrointestinal disorders			
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
Abdominal distension subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 24 (0.00%) 0	3 / 70 (4.29%) 3
Abdominal pain subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	1 / 24 (4.17%) 1	9 / 70 (12.86%) 12
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	3 / 70 (4.29%) 4
Aphthous ulcer subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
Ascites subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 24 (4.17%) 1	2 / 70 (2.86%) 2
Bowel movement irregularity subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 24 (0.00%) 0	1 / 70 (1.43%) 1
Constipation subjects affected / exposed occurrences (all)	5 / 18 (27.78%) 6	4 / 24 (16.67%) 6	14 / 70 (20.00%) 19
Diarrhoea subjects affected / exposed occurrences (all)	8 / 18 (44.44%) 15	10 / 24 (41.67%) 16	26 / 70 (37.14%) 41
Dry mouth subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 24 (0.00%) 0	2 / 70 (2.86%) 2
Dyspepsia			

subjects affected / exposed	5 / 18 (27.78%)	4 / 24 (16.67%)	10 / 70 (14.29%)
occurrences (all)	6	4	11
Dysphagia			
subjects affected / exposed	0 / 18 (0.00%)	2 / 24 (8.33%)	2 / 70 (2.86%)
occurrences (all)	0	2	2
Epigastric discomfort			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Eructation			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	2 / 70 (2.86%)
occurrences (all)	0	1	2
Faeces soft			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	3 / 70 (4.29%)
occurrences (all)	0	1	3
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 18 (5.56%)	4 / 24 (16.67%)	6 / 70 (8.57%)
occurrences (all)	1	4	7
Haemorrhoids			
subjects affected / exposed	2 / 18 (11.11%)	0 / 24 (0.00%)	4 / 70 (5.71%)
occurrences (all)	2	0	4
Mouth ulceration			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	12 / 18 (66.67%)	17 / 24 (70.83%)	45 / 70 (64.29%)
occurrences (all)	16	22	55
Odynophagia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Oesophagitis			
subjects affected / exposed	1 / 18 (5.56%)	1 / 24 (4.17%)	2 / 70 (2.86%)
occurrences (all)	1	1	2
Oral pain			

subjects affected / exposed	1 / 18 (5.56%)	1 / 24 (4.17%)	5 / 70 (7.14%)
occurrences (all)	1	1	5
Stomatitis			
subjects affected / exposed	6 / 18 (33.33%)	5 / 24 (20.83%)	14 / 70 (20.00%)
occurrences (all)	8	7	19
Vomiting			
subjects affected / exposed	5 / 18 (27.78%)	8 / 24 (33.33%)	21 / 70 (30.00%)
occurrences (all)	6	9	33
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	4 / 18 (22.22%)	1 / 24 (4.17%)	6 / 70 (8.57%)
occurrences (all)	4	1	7
Dermatitis allergic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Dry skin			
subjects affected / exposed	0 / 18 (0.00%)	6 / 24 (25.00%)	7 / 70 (10.00%)
occurrences (all)	0	6	7
Eczema			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Erythema			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	2 / 70 (2.86%)
occurrences (all)	0	1	2
Madarosis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Nail disorder			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Pruritus			

subjects affected / exposed	2 / 18 (11.11%)	8 / 24 (33.33%)	18 / 70 (25.71%)
occurrences (all)	5	10	30
Rash			
subjects affected / exposed	8 / 18 (44.44%)	10 / 24 (41.67%)	21 / 70 (30.00%)
occurrences (all)	13	17	36
Rash maculo-papular			
subjects affected / exposed	1 / 18 (5.56%)	4 / 24 (16.67%)	5 / 70 (7.14%)
occurrences (all)	1	5	6
Rash pruritic			
subjects affected / exposed	1 / 18 (5.56%)	1 / 24 (4.17%)	2 / 70 (2.86%)
occurrences (all)	1	1	2
Skin discolouration			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Skin exfoliation			
subjects affected / exposed	1 / 18 (5.56%)	1 / 24 (4.17%)	2 / 70 (2.86%)
occurrences (all)	1	1	2
Skin hypopigmentation			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Skin irritation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Vitiligo			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	2
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Chromaturia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1

Dysuria			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	3 / 70 (4.29%)
occurrences (all)	0	1	4
Nocturia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Strangury			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Urinary hesitation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 18 (11.11%)	5 / 24 (20.83%)	13 / 70 (18.57%)
occurrences (all)	4	7	22
Back pain			
subjects affected / exposed	1 / 18 (5.56%)	4 / 24 (16.67%)	9 / 70 (12.86%)
occurrences (all)	1	4	12
Bone pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	2
Joint swelling			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Muscle spasms			
subjects affected / exposed	0 / 18 (0.00%)	4 / 24 (16.67%)	5 / 70 (7.14%)
occurrences (all)	0	4	5
Muscular weakness			

subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	2 / 70 (2.86%)
occurrences (all)	1	0	2
Musculoskeletal chest pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	2 / 70 (2.86%)
occurrences (all)	1	0	2
Musculoskeletal pain			
subjects affected / exposed	0 / 18 (0.00%)	2 / 24 (8.33%)	6 / 70 (8.57%)
occurrences (all)	0	2	6
Myalgia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	4 / 70 (5.71%)
occurrences (all)	0	1	4
Neck pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Osteonecrosis of jaw			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Pain in extremity			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	5 / 70 (7.14%)
occurrences (all)	0	1	5
Pain in jaw			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Scoliosis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Infections and infestations			
Catheter site infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Conjunctivitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	2 / 70 (2.86%)
occurrences (all)	0	1	3
Ear infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1

Ear infection fungal			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Escherichia infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Escherichia urinary tract infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Hepatitis B			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Herpes simplex			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Herpes virus infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Influenza			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	3 / 70 (4.29%)
occurrences (all)	0	1	4
Mastitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 18 (5.56%)	1 / 24 (4.17%)	4 / 70 (5.71%)
occurrences (all)	1	1	5
Oral candidiasis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Pneumonia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 24 (4.17%)	2 / 70 (2.86%)
occurrences (all)	1	1	2

Tinea infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	3 / 18 (16.67%)	1 / 24 (4.17%)	7 / 70 (10.00%)
occurrences (all)	3	1	7
Urinary tract infection			
subjects affected / exposed	0 / 18 (0.00%)	2 / 24 (8.33%)	2 / 70 (2.86%)
occurrences (all)	0	3	3
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 18 (33.33%)	11 / 24 (45.83%)	25 / 70 (35.71%)
occurrences (all)	6	13	28
Dehydration			
subjects affected / exposed	1 / 18 (5.56%)	3 / 24 (12.50%)	4 / 70 (5.71%)
occurrences (all)	1	3	4
Hypercalcaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	2 / 70 (2.86%)
occurrences (all)	1	0	2
Hypercholesterolaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Hyperglycaemia			
subjects affected / exposed	12 / 18 (66.67%)	9 / 24 (37.50%)	23 / 70 (32.86%)
occurrences (all)	18	15	35
Hyperkalaemia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 24 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Hypermagnesaemia			

subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Hypernatraemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Hypoalbuminaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 24 (0.00%)	3 / 70 (4.29%)
occurrences (all)	1	0	3
Hypocalcaemia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 24 (4.17%)	2 / 70 (2.86%)
occurrences (all)	1	1	2
Hypoglycaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 24 (4.17%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Hypokalaemia			
subjects affected / exposed	2 / 18 (11.11%)	3 / 24 (12.50%)	6 / 70 (8.57%)
occurrences (all)	2	3	6
Hypomagnesaemia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 24 (4.17%)	3 / 70 (4.29%)
occurrences (all)	1	1	3
Hyponatraemia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 24 (4.17%)	4 / 70 (5.71%)
occurrences (all)	1	1	4
Hypophosphataemia			
subjects affected / exposed	0 / 18 (0.00%)	3 / 24 (12.50%)	3 / 70 (4.29%)
occurrences (all)	0	3	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 July 2014	The purpose of this amendment was to appropriately manage the safety of patients while on the study medications .Changes were made to the inclusion/exclusion criteria to raise the ANC Level, the option to explore additional schedules was clarified, Concomitant medication exclusions were modified, Hyperglycemia and alanine aminotransferase (ALT) DLT criterion were modified.
08 January 2015	The purpose of this amendment was to include guidelines for management of pneumonitis. This was due to an urgent safety measure issued in response to cases of pneumonitis observed in patients being treated with BYL719.
11 November 2015	Main changes were : - Updated hepatic monitoring plan, and to provide additional guidance for BKM120 and ribociclib dose modifications related to hepatotoxicity. - Updated cardiac monitoring plan, and to provide additional guidance on dose modifications for ribociclib related cardiotoxicities.
29 March 2016	The main purpose of this amendment was to correct a clerical error in the previous version of the protocol within the criteria for discontinuation language in Appendix 16.1.1-Section 7.1.4 (Discontinuation of treatment).
15 November 2016	The main purpose of this amendment was to provide updated guidelines when a patient exhibits suicidal ideation and increase patient safety Provide updated study drug administration guidelines and in particular food administration recommendations for LEE011, BKM120 and BYL719 Provide updated guidelines on discontinuation of study treatment, following a Health Authority request. They include modifications to the sections outlining the reasons where study treatment may be discontinued and, where study treatment must be discontinued. An additional statement regarding ongoing patients continuing in an LEE011 rollover protocol has also been added. Clarify the definition of dose limiting toxicities (DLTs) to indicate that a DLT occurs during the first 28 days of dosing (Cycle 1). Provide updated study drug guidelines for ongoing patients who may continue treatment in an LEE011 rollover protocol

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Novartis made the decision to not open the Phase II portion of the study, for business reasons. Sufficient data had already been collected and no additional data for the triplet combinations was needed.

Notes: