Clinical trial results:
A phase Ib/II, open-label study of LJM716 in combination with BYL719 compared to taxane or irinotecan in patients with previously treated esophageal squamous cell carcinoma

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results.

Summary

EudraCT number	2012-005624-15
Trial protocol	ES BE GB FR
Global end of trial date	03 June 2016
Results information	
Result version number	v1 (current)
This version publication date	11 July 2018
First version publication date	11 July 2018

Trial information

Trial identification	
Sponsor protocol code	CLJM716X2103
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01822613
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,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

Notes:

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 June 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 June 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To study the safety and efficacy of the combination of LJM716 and BYL719 against currently available treatments of physician’s choice in previously treated ESCC patients

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	26 July 2013
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	Canada: 1
Country: Number of subjects enrolled	Hong Kong: 1
Country: Number of subjects enrolled	Korea, Republic of: 11
Country: Number of subjects enrolled	Singapore: 4
Country: Number of subjects enrolled	Taiwan: 19
Country: Number of subjects enrolled	United States: 3
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Belgium: 3
Worldwide total number of subjects	48
EEA total number of subjects	9

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)	30
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study design included a Phase 1b dose escalation portion to define the maximum tolerated dose (MTD)/recommended phase 2 dose (RP2D) for the combination of LJM716 and alpelisib, followed by an open-label, randomized Phase 2 part to compare anti-tumor activity of LJM716-alpelisib combination versus physician's choice of second-line therapy.

Pre-assignment

Screening details:

The phase 2 part was not conducted as the study was terminated early due to limited anti-tumor activity with LJM716-alpelisib combination observed in phase 1b.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	LJM716 10/kg qw + BYL719 300 mg/day

Arm description:

LJM716 10 mg/kg was given as a once weekly infusion beginning on cycle 1 day 1. BYL719 300 mg was administered orally on a once daily schedule starting cycle 1 day 1.

Arm type	Experimental
Investigational medicinal product name	LJM716
Investigational medicinal product code	LJM716
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

LJM716 10 mg/kg was given as a once weekly infusion beginning on cycle 1 day 1.

Investigational medicinal product name	BYL719
Investigational medicinal product code	BYL719
Other name	Alpelisib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

BYL719 300 mg was administered orally on a once daily schedule starting cycle 1 day 1.

Arm title	LJM716 20 mg/kg qw + BYL719 300 mg/day

Arm description:

LJM716 20 mg/kg was given as a once weekly infusion beginning on cycle 1 day 1. BYL719 300 mg was administered orally on a once daily schedule starting cycle 1 day 1.

Arm type	Experimental

Investigational medicinal product name	LJM716
Investigational medicinal product code	LJM716
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

LJM716 20 mg/kg was given as a once weekly infusion beginning on cycle 1 day 1.

Investigational medicinal product name	BYL719
Investigational medicinal product code	BYL719
Other name	Alpelisib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

BYL719 300 mg was administered orally on a once daily schedule starting cycle 1 day 1.

Arm title	LJM716 30 mg/kg qw + BYL719 250 mg/day

Arm description:

LJM716 30 mg/kg was given as a once weekly infusion beginning on cycle 1 day 1. BYL719 250 mg was administered orally on a once daily schedule starting cycle 1 day 1.

Arm type	Experimental
Investigational medicinal product name	LJM716
Investigational medicinal product code	LJM716
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

LJM716 30 mg/kg was given as a once weekly infusion beginning on cycle 1 day 1.

Investigational medicinal product name	BYL719
Investigational medicinal product code	BYL719
Other name	Alpelisib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

BYL719 250 mg was administered orally on a once daily schedule starting cycle 1 day 1.

Arm title	LJM716 30 mg/kg + BYL719 300 mg/day

Arm description:

LJM716 30 mg/kg was given as a once weekly infusion beginning on cycle 1 day 1. BYL719 300 mg was administered orally on a once daily schedule starting cycle 1 day 1.

Arm type	Experimental
Investigational medicinal product name	LJM716
Investigational medicinal product code	LJM716
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

LJM716 30 mg/kg was given as a once weekly infusion beginning on cycle 1 day 1.

Investigational medicinal product name	BYL719
Investigational medicinal product code	BYL719
Other name	Alpelisib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

BYL719 300 mg was administered orally on a once daily schedule starting cycle 1 day 1.

Number of subjects in period 1	LJM716 10/kg qw + BYL719 300 mg/day	LJM716 20 mg/kg qw + BYL719 300 mg/day	LJM716 30 mg/kg qw + BYL719 250 mg/day
Started	14	15	11
Dose determining analysis set	10	10	9
Full analysis set	14	15	11
Safety set	14	15	11
Completed	0	0	0
Not completed	14	15	11
Physician decision	2	1	-
Consent withdrawn by subject	2	1	1
Adverse event, non-fatal	1	4	2
Technical problems	1	-	-
Death	-	2	-
Progressive disease	8	7	8

Number of subjects in period 1	LJM716 30 mg/kg + BYL719 300 mg/day
Started	8
Dose determining analysis set	6
Full analysis set	8
Safety set	8
Completed	0
Not completed	8
Physician decision	2
Consent withdrawn by subject	-
Adverse event, non-fatal	1
Technical problems	-
Death	-
Progressive disease	5

Baseline characteristics

Reporting groups	
Reporting group title	LJM716 10/kg qw + BYL719 300 mg/day
Reporting group description:	
LJM716 10 mg/kg was given as a once weekly infusion beginning on cycle 1 day 1. BYL719 300 mg was administered orally on a once daily schedule starting cycle 1 day 1.	

Reporting group title	LJM716 20 mg/kg qw + BYL719 300 mg/day
Reporting group description:	
LJM716 20 mg/kg was given as a once weekly infusion beginning on cycle 1 day 1. BYL719 300 mg was administered orally on a once daily schedule starting cycle 1 day 1.	
Reporting group title	LJM716 30 mg/kg qw + BYL719 250 mg/day
Reporting group description:	
LJM716 30 mg/kg was given as a once weekly infusion beginning on cycle 1 day 1. BYL719 250 mg was administered orally on a once daily schedule starting cycle 1 day 1.	
Reporting group title	LJM716 30 mg/kg + BYL719 300 mg/day
Reporting group description:	
LJM716 30 mg/kg was given as a once weekly infusion beginning on cycle 1 day 1. BYL719 300 mg was administered orally on a once daily schedule starting cycle 1 day 1.	

Reporting group values	LJM716 10/kg qw + BYL719 300 mg/day	LJM716 20 mg/kg qw + BYL719 300 mg/day	LJM716 30 mg/kg qw + BYL719 250 mg/day
Number of subjects	14	15	11
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	12	6
From 65-84 years	6	3	5
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	61.6	55.5	61.5
standard deviation	± 8.12	± 11.41	± 6.47
Gender categorical			
Units: Subjects			
Female	4	0	2
Male	10	15	9

Reporting group values	LJM716 30 mg/kg + BYL719 300 mg/day	Total	
Number of subjects	8	48	

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)	4	30	
From 65-84 years	4	18	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	61.8		
standard deviation	± 6.88	-	
Gender categorical Units: Subjects			
Female	2	8	
Male	6	40	

End points

End points reporting groups

Reporting group title	LJM716 10/kg qw + BYL719 300 mg/day

Reporting group description:

LJM716 10 mg/kg was given as a once weekly infusion beginning on cycle 1 day 1. BYL719 300 mg was administered orally on a once daily schedule starting cycle 1 day 1.

Reporting group title	LJM716 20 mg/kg qw + BYL719 300 mg/day

Reporting group description:

LJM716 20 mg/kg was given as a once weekly infusion beginning on cycle 1 day 1. BYL719 300 mg was administered orally on a once daily schedule starting cycle 1 day 1.

Reporting group title	LJM716 30 mg/kg qw + BYL719 250 mg/day

Reporting group description:

LJM716 30 mg/kg was given as a once weekly infusion beginning on cycle 1 day 1. BYL719 250 mg was administered orally on a once daily schedule starting cycle 1 day 1.

Reporting group title	LJM716 30 mg/kg + BYL719 300 mg/day

Reporting group description:

LJM716 30 mg/kg was given as a once weekly infusion beginning on cycle 1 day 1. BYL719 300 mg was administered orally on a once daily schedule starting cycle 1 day 1.

Primary: Number of participants with dose limiting toxicities (DLTs)

End point title	Number of participants with dose limiting toxicities (DLTs)[1]

End point description:

The incidence of DLTs was assessed. The dose determining set (DDS) was analyzed. The DDS included all participants from the safety set who either completed a minimum exposure requirement and had sufficient safety evaluations or discontinued prematurely due to a DLT during the DLT assessment period. The DLT assessment period was defined as the 28-day period beginning with the first dose of study drug. The safety set included all participants who received at least one dose of alpelisib or LJM716, and had at least one valid post-baseline safety assessment.

End point type	Primary

End point timeframe:

8 months

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: Descriptive summary statistics only apply to this end point.

End point values	LJM716 10/kg qw + BYL719 300 mg/day	LJM716 20 mg/kg qw + BYL719 300 mg/day	LJM716 30 mg/kg qw + BYL719 250 mg/day	LJM716 30 mg/kg + BYL719 300 mg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	9	6
Units: Participants				
Participants with at least one event	3	3	2	2
Decreased appetite	0	1	0	0
Fatigue	1	0	0	0
Hyperbilirubinaemia	0	1	0	0
Hyperglycaemia	2	1	2	1
Vomiting	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with best overall response (BOR)

End point title	Number of participants with best overall response (BOR)

End point description:

The number of participants with complete response (CR), partial response (PR), stable disease (SD), progressive disease (PD) or unknown status was assessed. BOR was based on Investigator's assessment of disease status using Response Evaluation Criteria In Solid Tumors (RECIST) 1.1.

End point type	Secondary

End point timeframe:

about 4 months

End point values	LJM716 10/kg qw + BYL719 300 mg/day	LJM716 20 mg/kg qw + BYL719 300 mg/day	LJM716 30 mg/kg qw + BYL719 250 mg/day	LJM716 30 mg/kg + BYL719 300 mg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	15	11	8
Units: Participants				
CR	0	0	0	0
PR	0	4	1	1
SD	4	2	3	1
PD	6	7	6	4
Unknown	4	2	1	2

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response rate (ORR)

End point title	Overall response rate (ORR)

End point description:

End point type	Secondary

End point timeframe:

The number of participants with CR or PR was assessed.

End point values	LJM716 10/kg qw + BYL719 300 mg/day	LJM716 20 mg/kg qw + BYL719 300 mg/day	LJM716 30 mg/kg qw + BYL719 250 mg/day	LJM716 30 mg/kg + BYL719 300 mg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	15	11	8
Units: Participants	0	4	1	1

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control rate (DCR)

End point title	Disease control rate (DCR)

End point description:

End point type	Secondary

End point timeframe:

The number of participants with CR, PR or SD was assessed.

End point values	LJM716 10/kg qw + BYL719 300 mg/day	LJM716 20 mg/kg qw + BYL719 300 mg/day	LJM716 30 mg/kg qw + BYL719 250 mg/day	LJM716 30 mg/kg + BYL719 300 mg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	15	11	8
Units: Participants	4	6	4	2

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS)

End point title	Progression free survival (PFS)

End point description:

PFS was defined as the time from the date of randomization to the date of first radiologically documented progression or death due to any cause.

End point type	Secondary

End point timeframe:

about 5 months

End point values	LJM716 10/kg qw + BYL719 300 mg/day	LJM716 20 mg/kg qw + BYL719 300 mg/day	LJM716 30 mg/kg qw + BYL719 250 mg/day	LJM716 30 mg/kg + BYL719 300 mg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	15	11	8
Units: months				
median (confidence interval 95%)	2.3 (1.31 to 4.96)	1.86 (1.08 to 4.14)	2.56 (1.22 to 4.07)	1.94 (1.18 to 3.06)

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter for LJM716: AUClast

End point title	PK parameter for LJM716: AUClast

End point description:

AUClast = the area under the concentration-time curve from time zero to the last measurable concentration time sampling. Participants with non-missing values were analyzed.

End point type	Secondary

End point timeframe:

Cycle 1, day and cycle 3, day 1

End point values	LJM716 10/kg qw + BYL719 300 mg/day	LJM716 20 mg/kg qw + BYL719 300 mg/day	LJM716 30 mg/kg qw + BYL719 250 mg/day	LJM716 30 mg/kg + BYL719 300 mg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	15	11	8
Units: hr*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1, day 1 (n=10,11,9,6)	18569 (± 5373)	32679 (± 7010)	56503 (± 8979)	51053 (± 5663)
Cycle 3, day 1 (n=4,4,3,1)	49069 (± 12677)	71939 (± 29197)	131967 (± 20983)	172205 (± 9999)

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter for LJM716: Cmax

End point title	PK parameter for LJM716: Cmax

End point description:

Cmax = maximum observed concentration after drug administration. Participants with non-missing values were analyzed.

End point type	Secondary

End point timeframe:

Cycle 1, day 1 and cycle 3, day 1

End point values	LJM716 10/kg qw + BYL719 300 mg/day	LJM716 20 mg/kg qw + BYL719 300 mg/day	LJM716 30 mg/kg qw + BYL719 250 mg/day	LJM716 30 mg/kg + BYL719 300 mg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	15	11	8
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1, day 1 (n=13,13,10,8)	196 (± 43)	364 (± 91.2)	597 (± 87)	561 (± 85.2)
Cycle 3, day 1 (n=7,5,5,3)	356 (± 125)	660 (± 203)	1106 (± 189)	1143 (± 150)

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter for for BYL719 (alpelisib): AUClast

End point title	PK parameter for for BYL719 (alpelisib): AUClast

End point description:

AUClast = the area under the concentration-time curve from time zero to the last measurable concentration sampling time. Participants with non-missing values were analyzed.

End point type	Secondary

End point timeframe:

Cycle 1, day 1 and cycle 3, day 1

End point values	LJM716 10/kg qw + BYL719 300 mg/day	LJM716 20 mg/kg qw + BYL719 300 mg/day	LJM716 30 mg/kg qw + BYL719 250 mg/day	LJM716 30 mg/kg + BYL719 300 mg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	15	11	8
Units: hr*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1, day 1 (n=12,11,9,5)	21860 (± 12022)	23121 (± 10830)	19944 (± 9389)	26814 (± 4462)
Cycle 3, day 1 (n=4,4,3,1)	21344 (± 13343)	21819 (± 8394)	23164 (± 6419)	24275 (± 9999)

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter for BYL719 (alpelisib): Cmax

End point title	PK parameter for BYL719 (alpelisib): Cmax

End point description:

Cmax = maximum observed concentration after drug administration. Participants with non-missing values were analyzed.

End point type	Secondary

End point timeframe:

Cycle 1, day 1 and cycle 3, day 1

End point values	LJM716 10/kg qw + BYL719 300 mg/day	LJM716 20 mg/kg qw + BYL719 300 mg/day	LJM716 30 mg/kg qw + BYL719 250 mg/day	LJM716 30 mg/kg + BYL719 300 mg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	15	11	8
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1, day 1 (n=14,13,11,6)	1873 (± 1119)	2147 (± 1046)	1478 (± 645)	2208 (± 493)
Cycle 3, day 1 (n=5,5,5,3)	1579 (± 1051)	1444 (± 1001)	1582 (± 610)	1873 (± 1081)

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter for BYL719 (alpelisib): Tmax

End point title	PK parameter for BYL719 (alpelisib): Tmax

End point description:

Tmax = the time to reach the maximum concentration after drug administration. Participants with non-missing values were analyzed.

End point type	Secondary

End point timeframe:

Cycle 1, day 1 and cycle 3, day 1

End point values	LJM716 10/kg qw + BYL719 300 mg/day	LJM716 20 mg/kg qw + BYL719 300 mg/day	LJM716 30 mg/kg qw + BYL719 250 mg/day	LJM716 30 mg/kg + BYL719 300 mg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	15	11	8
Units: hour				
median (full range (min-max))				

Cycle 1, day 1 (n=14,4,4,4)	4 (1.97 to 7.95)	4 (1.9 to 8.68)	4 (2 to 7)	4 (1.92 to 7.98)
Cycle 3, day 1 (n=5,5,5,3)	4 (1.98 to 23.9)	4.17 (1.85 to 23.8)	2 (0.5 to 7.4)	4.15 (2 to 7.93)

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter for BYL719 (alpelisib): AUCinf

End point title	PK parameter for BYL719 (alpelisib): AUCinf

End point description:

AUCinf = the area under the concentration-time curve from time zero to infinity. Participants with non-missing values were analyzed.

End point type	Secondary

End point timeframe:

Cycle 1, day 1 and cycle 3, day 1

End point values	LJM716 10/kg qw + BYL719 300 mg/day	LJM716 20 mg/kg qw + BYL719 300 mg/day	LJM716 30 mg/kg qw + BYL719 250 mg/day	LJM716 30 mg/kg + BYL719 300 mg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	15	11	8
Units: hr*ng/mL				
arithmetic mean (standard deviation)				
Cycle 1, day 1 (n=6,5,5,3)	31082 (± 8890)	28498 (± 12438)	19192 (± 7395)	28165 (± 3122)
Cycle 3, day 1(n=2,1,2,1)	13515 (± 10898)	32305 (± 9999)	23910 (± 8299)	24961 (± 9999)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	LJM716 10 mg/kg QW@+ BYL719 300 mg/day
Reporting group description:	
LJM716 10 mg/kg QW@+ BYL719 300 mg/day	
Reporting group title	LJM716 20 mg/kg QW@+ BYL719 300 mg/day
Reporting group description:	
LJM716 20 mg/kg QW@+ BYL719 300 mg/day	
Reporting group title	LJM716 30 mg/kg QW@+ BYL719 250 mg/day
Reporting group description:	
LJM716 30 mg/kg QW@+ BYL719 250 mg/day	
Reporting group title	LJM716 30 mg/kg QW@+ BYL719 300 mg/day
Reporting group description:	
LJM716 30 mg/kg QW@+ BYL719 300 mg/day	
Reporting group title	All@patients
Reporting group description:	
All@patients	

Serious adverse events	LJM716 10 mg/kg QW@+ BYL719 300 mg/day	LJM716 20 mg/kg QW@+ BYL719 300 mg/day	LJM716 30 mg/kg QW@+ BYL719 250 mg/day
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 14 (92.86%)	9 / 15 (60.00%)	4 / 11 (36.36%)
number of deaths (all causes)	5	3	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
TUMOUR NECROSIS			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (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

General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (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
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY DISTRESS SYNDROME			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
DYSPNOEA			
subjects affected / exposed	1 / 14 (7.14%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
HAEMOPTYSIS			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (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
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
OESOPHAGOBRONCHIAL FISTULA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (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
PLEURAL FISTULA			

subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (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
PNEUMOMEDIASTINUM			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
PNEUMONIA ASPIRATION			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOTHORAX			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
RESPIRATORY FAILURE			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
COMPLETED SUICIDE			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (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			
WEIGHT DECREASED			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (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
Congenital, familial and genetic disorders			
TRACHEO-OESOPHAGEAL FISTULA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
ARRHYTHMIA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDIAL EFFUSION			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (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
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (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			
BRAIN INJURY			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
COMA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (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			
AORTO-OESOPHAGEAL FISTULA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (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
DIARRHOEA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (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
DYSPHAGIA			

subjects affected / exposed	1 / 14 (7.14%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ULCER			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (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
OESOPHAGEAL ACHALASIA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OESOPHAGEAL FISTULA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
OESOPHAGEAL PERFORATION			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
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 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STOMATITIS			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (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
VOMITING			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (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
Skin and subcutaneous tissue disorders			
SUBCUTANEOUS EMPHYSEMA			

subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (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 OBSTRUCTION			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUSCULOSKELETAL PAIN			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (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
Infections and infestations			
ARTHRITIS BACTERIAL			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (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
BACTERAEMIA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (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

CYSTITIS			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (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
LUNG INFECTION			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (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	1 / 14 (7.14%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
RESPIRATORY SYNCYTIAL VIRUS INFECTION			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (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 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (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
SEPTIC SHOCK			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (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

DEHYDRATION			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (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
HYPERCALCAEMIA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (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
HYPERGLYCAEMIA			
subjects affected / exposed	2 / 14 (14.29%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOPHAGIA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	LJM716 30 mg/kg QW@+ BYL719 300 mg/day	All@patients	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 8 (75.00%)	32 / 48 (66.67%)	
number of deaths (all causes)	0	9	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
TUMOUR NECROSIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			

ACUTE RESPIRATORY DISTRESS SYNDROME			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
DYSPNOEA			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
HAEMOPTYSIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
OESOPHAGOBRONCHIAL FISTULA			
subjects affected / exposed	1 / 8 (12.50%)	2 / 48 (4.17%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURAL FISTULA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMOMEDIASTINUM			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
PNEUMONIA ASPIRATION			

subjects affected / exposed	1 / 8 (12.50%)	3 / 48 (6.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMOTHORAX			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
RESPIRATORY FAILURE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
COMPLETED SUICIDE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
WEIGHT DECREASED			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
TRACHEO-OESOPHAGEAL FISTULA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ARRHYTHMIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDIAL EFFUSION			

subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
BRAIN INJURY			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
COMA			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Gastrointestinal disorders			
AORTO-OESOPHAGEAL FISTULA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPHAGIA			
subjects affected / exposed	1 / 8 (12.50%)	4 / 48 (8.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRIC ULCER			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
OESOPHAGEAL ACHALASIA			

subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
OESOPHAGEAL FISTULA			
subjects affected / exposed	1 / 8 (12.50%)	2 / 48 (4.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
OESOPHAGEAL PERFORATION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
STOMATITIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			
subjects affected / exposed	1 / 8 (12.50%)	2 / 48 (4.17%)	
occurrences causally related to treatment / all	1 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
SUBCUTANEOUS EMPHYSEMA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT OBSTRUCTION			

subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
ARTHRITIS BACTERIAL			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACTERAEMIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHITIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CYSTITIS			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
LUNG INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

PNEUMONIA			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
RESPIRATORY SYNCYTIAL VIRUS INFECTION			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPTIC SHOCK			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEHYDRATION			
subjects affected / exposed	1 / 8 (12.50%)	2 / 48 (4.17%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERCALCAEMIA			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

HYPERGLYCAEMIA			
subjects affected / exposed	1 / 8 (12.50%)	3 / 48 (6.25%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOPHAGIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	LJM716 10 mg/kg QW@+ BYL719 300 mg/day	LJM716 20 mg/kg QW@+ BYL719 300 mg/day	LJM716 30 mg/kg QW@+ BYL719 250 mg/day
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)	15 / 15 (100.00%)	11 / 11 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
CANCER PAIN			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
TUMOUR PAIN			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
HAEMATOMA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
HYPERTENSION			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences (all)	0	1	2
HYPOTENSION			
subjects affected / exposed	2 / 14 (14.29%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
General disorders and administration site conditions			
ASTHENIA			

subjects affected / exposed	2 / 14 (14.29%)	3 / 15 (20.00%)	0 / 11 (0.00%)
occurrences (all)	2	3	0
CHEST DISCOMFORT			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
CHILLS			
subjects affected / exposed	1 / 14 (7.14%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences (all)	2	1	1
FATIGUE			
subjects affected / exposed	6 / 14 (42.86%)	5 / 15 (33.33%)	6 / 11 (54.55%)
occurrences (all)	8	15	7
GENERALISED OEDEMA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
MALAISE			
subjects affected / exposed	3 / 14 (21.43%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	3	1	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	2 / 14 (14.29%)	4 / 15 (26.67%)	0 / 11 (0.00%)
occurrences (all)	2	4	0
OEDEMA PERIPHERAL			
subjects affected / exposed	1 / 14 (7.14%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences (all)	3	1	1
PAIN			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
PERIPHERAL SWELLING			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
PYREXIA			
subjects affected / exposed	5 / 14 (35.71%)	5 / 15 (33.33%)	1 / 11 (9.09%)
occurrences (all)	10	6	1
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0

Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	5 / 14 (35.71%)	3 / 15 (20.00%)	2 / 11 (18.18%)
occurrences (all)	5	4	2
DYSPHONIA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
DYSPNOEA			
subjects affected / exposed	5 / 14 (35.71%)	3 / 15 (20.00%)	1 / 11 (9.09%)
occurrences (all)	5	4	1
DYSPNOEA EXERTIONAL			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
EPISTAXIS			
subjects affected / exposed	0 / 14 (0.00%)	2 / 15 (13.33%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
HAEMOPTYSIS			
subjects affected / exposed	1 / 14 (7.14%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
HICCUPS			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
HYPOXIA			
subjects affected / exposed	2 / 14 (14.29%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
PLEURAL EFFUSION			
subjects affected / exposed	1 / 14 (7.14%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
PLEURISY			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
PNEUMONIA ASPIRATION			

subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
PNEUMONITIS			
subjects affected / exposed	2 / 14 (14.29%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
PRODUCTIVE COUGH			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
RHINITIS ALLERGIC			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
RHINORRHOEA			
subjects affected / exposed	0 / 14 (0.00%)	3 / 15 (20.00%)	0 / 11 (0.00%)
occurrences (all)	0	3	0
SPUTUM DISCOLOURED			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
DEPRESSED MOOD			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
DEPRESSION			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
INSOMNIA			
subjects affected / exposed	0 / 14 (0.00%)	2 / 15 (13.33%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			

subjects affected / exposed	1 / 14 (7.14%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
AMYLASE INCREASED			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences (all)	0	1	2
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 14 (7.14%)	2 / 15 (13.33%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
BILIRUBIN CONJUGATED INCREASED			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
BLOOD CHOLESTEROL INCREASED			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
BLOOD CREATINE INCREASED			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
BLOOD CREATININE INCREASED			
subjects affected / exposed	2 / 14 (14.29%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	2	2	0
ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
LIPASE INCREASED			

subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
TROPONIN I INCREASED			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
TROPONIN INCREASED			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
WEIGHT DECREASED			
subjects affected / exposed	7 / 14 (50.00%)	8 / 15 (53.33%)	5 / 11 (45.45%)
occurrences (all)	7	10	6
Injury, poisoning and procedural complications			
INFUSION RELATED REACTION			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
SCRATCH			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
STOMA SITE HAEMORRHAGE			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
ATRIOVENTRICULAR BLOCK FIRST DEGREE			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
SINUS BRADYCARDIA			

subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
SINUS TACHYCARDIA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
TACHYCARDIA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
DYSGEUSIA			
subjects affected / exposed	1 / 14 (7.14%)	1 / 15 (6.67%)	2 / 11 (18.18%)
occurrences (all)	1	1	2
HEADACHE			
subjects affected / exposed	0 / 14 (0.00%)	2 / 15 (13.33%)	0 / 11 (0.00%)
occurrences (all)	0	3	0
LETHARGY			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
POLYNEUROPATHY			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
SOMNOLENCE			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	4 / 14 (28.57%)	0 / 15 (0.00%)	2 / 11 (18.18%)
occurrences (all)	5	0	2
LEUKOCYTOSIS			

subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
NEUTROPENIA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
PANCYTOPENIA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
DRY EYE			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
EYE DISCHARGE			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
VISION BLURRED			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
ABDOMINAL PAIN			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	3
ABDOMINAL PAIN UPPER			
subjects affected / exposed	2 / 14 (14.29%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
ASCITES			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
CHEILITIS			

subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
CONSTIPATION			
subjects affected / exposed	1 / 14 (7.14%)	4 / 15 (26.67%)	0 / 11 (0.00%)
occurrences (all)	1	10	0
DIARRHOEA			
subjects affected / exposed	12 / 14 (85.71%)	12 / 15 (80.00%)	10 / 11 (90.91%)
occurrences (all)	21	22	29
DRY MOUTH			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
DYSPEPSIA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
DYSPHAGIA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
GASTRITIS EROSIVE			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
GINGIVAL PAIN			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
GLOSSODYNIA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
HAEMORRHOIDS			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
LIP PAIN			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

MEGACOLON			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
NAUSEA			
subjects affected / exposed	4 / 14 (28.57%)	3 / 15 (20.00%)	3 / 11 (27.27%)
occurrences (all)	4	3	4
OESOPHAGEAL ACHALASIA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
OESOPHAGEAL PAIN			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
PROCTALGIA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
STOMATITIS			
subjects affected / exposed	6 / 14 (42.86%)	6 / 15 (40.00%)	5 / 11 (45.45%)
occurrences (all)	6	6	5
TOOTHACHE			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
VOMITING			
subjects affected / exposed	5 / 14 (35.71%)	3 / 15 (20.00%)	3 / 11 (27.27%)
occurrences (all)	6	3	4
Hepatobiliary disorders			
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
DECUBITUS ULCER			

subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
DERMATITIS ACNEIFORM			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
DRY SKIN			
subjects affected / exposed	1 / 14 (7.14%)	1 / 15 (6.67%)	2 / 11 (18.18%)
occurrences (all)	1	1	2
ECCHYMOSIS			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
ECZEMA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
ERYTHEMA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
NAIL TOXICITY			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
PETECHIAE			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
PRURIGO			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
PRURITUS			
subjects affected / exposed	2 / 14 (14.29%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	3
RASH			
subjects affected / exposed	3 / 14 (21.43%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	3	0	1
RASH ERYTHEMATOUS			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
RASH MACULAR			

subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
RASH MACULO-PAPULAR			
subjects affected / exposed	2 / 14 (14.29%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
RASH PAPULAR			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
SKIN HYPOPIGMENTATION			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
SKIN LESION			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
SKIN REACTION			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
SKIN ULCER			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
CHRONIC KIDNEY DISEASE			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
HAEMATURIA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
POLLAKIURIA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
URETHRAL PAIN			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
URINARY TRACT PAIN			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1

Endocrine disorders			
HYPOTHYROIDISM			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	1 / 14 (7.14%)	2 / 15 (13.33%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
FLANK PAIN			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
JOINT SWELLING			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
MUSCLE SPASMS			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	2 / 11 (18.18%)
occurrences (all)	0	1	2
MYOFASCIAL PAIN SYNDROME			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
NECK PAIN			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Infections and infestations			
ANGULAR CHEILITIS			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
BACTERAEMIA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

BRONCHITIS			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
CELLULITIS			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
CLOSTRIDIUM DIFFICILE COLITIS			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
HERPES ZOSTER			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
LICE INFESTATION			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
LIVER ABSCESS			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
LUNG INFECTION			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
ONYCHOMYCOSIS			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
ORAL CANDIDIASIS			
subjects affected / exposed	2 / 14 (14.29%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
OSTEOMYELITIS			

subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
PARONYCHIA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
RASH PUSTULAR			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
SINUSITIS			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
URETHRITIS			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
URINARY TRACT INFECTION			
subjects affected / exposed	2 / 14 (14.29%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
VULVOVAGINAL CANDIDIASIS			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	11 / 14 (78.57%)	8 / 15 (53.33%)	6 / 11 (54.55%)
occurrences (all)	12	10	6
DEHYDRATION			
subjects affected / exposed	1 / 14 (7.14%)	1 / 15 (6.67%)	2 / 11 (18.18%)
occurrences (all)	2	1	2
HYPERCALCAEMIA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
HYPERGLYCAEMIA			

subjects affected / exposed	8 / 14 (57.14%)	6 / 15 (40.00%)	5 / 11 (45.45%)
occurrences (all)	16	14	9
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	0 / 14 (0.00%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
HYPERURICAEMIA			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
HYPOALBUMINAEMIA			
subjects affected / exposed	1 / 14 (7.14%)	2 / 15 (13.33%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
HYPOCALCAEMIA			
subjects affected / exposed	1 / 14 (7.14%)	1 / 15 (6.67%)	1 / 11 (9.09%)
occurrences (all)	3	1	4
HYPOKALAEMIA			
subjects affected / exposed	3 / 14 (21.43%)	2 / 15 (13.33%)	1 / 11 (9.09%)
occurrences (all)	6	2	4
HYPOMAGNESAEMIA			
subjects affected / exposed	2 / 14 (14.29%)	2 / 15 (13.33%)	1 / 11 (9.09%)
occurrences (all)	3	2	3
HYPONATRAEMIA			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
HYPOPHAGIA			
subjects affected / exposed	2 / 14 (14.29%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
HYPOPHOSPHATAEMIA			
subjects affected / exposed	2 / 14 (14.29%)	0 / 15 (0.00%)	2 / 11 (18.18%)
occurrences (all)	2	0	6
METABOLIC ACIDOSIS			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	LJM716 30 mg/kg QW@+ BYL719 300 mg/day	All@patients	
Total subjects affected by non-serious adverse events			

subjects affected / exposed	8 / 8 (100.00%)	48 / 48 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
CANCER PAIN			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
TUMOUR PAIN			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
Vascular disorders			
HAEMATOMA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
HYPERTENSION			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	3	
HYPOTENSION			
subjects affected / exposed	0 / 8 (0.00%)	3 / 48 (6.25%)	
occurrences (all)	0	3	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 8 (0.00%)	5 / 48 (10.42%)	
occurrences (all)	0	5	
CHEST DISCOMFORT			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
CHILLS			
subjects affected / exposed	0 / 8 (0.00%)	3 / 48 (6.25%)	
occurrences (all)	0	4	
FATIGUE			
subjects affected / exposed	4 / 8 (50.00%)	21 / 48 (43.75%)	
occurrences (all)	4	34	
GENERALISED OEDEMA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
MALAISE			

subjects affected / exposed	0 / 8 (0.00%)	4 / 48 (8.33%)	
occurrences (all)	0	4	
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 8 (12.50%)	7 / 48 (14.58%)	
occurrences (all)	2	8	
OEDEMA PERIPHERAL			
subjects affected / exposed	1 / 8 (12.50%)	4 / 48 (8.33%)	
occurrences (all)	1	6	
PAIN			
subjects affected / exposed	2 / 8 (25.00%)	2 / 48 (4.17%)	
occurrences (all)	2	2	
PERIPHERAL SWELLING			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
PYREXIA			
subjects affected / exposed	2 / 8 (25.00%)	13 / 48 (27.08%)	
occurrences (all)	2	19	
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	6 / 8 (75.00%)	16 / 48 (33.33%)	
occurrences (all)	8	19	
DYSPHONIA			
subjects affected / exposed	1 / 8 (12.50%)	3 / 48 (6.25%)	
occurrences (all)	1	3	
DYSPNOEA			
subjects affected / exposed	2 / 8 (25.00%)	11 / 48 (22.92%)	
occurrences (all)	2	12	
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
EPISTAXIS			

subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
HAEMOPTYSIS			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
HICCUPS			
subjects affected / exposed	1 / 8 (12.50%)	2 / 48 (4.17%)	
occurrences (all)	1	2	
HYPOXIA			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
PLEURAL EFFUSION			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
PLEURISY			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
PNEUMONIA ASPIRATION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
PNEUMONITIS			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
PRODUCTIVE COUGH			
subjects affected / exposed	4 / 8 (50.00%)	5 / 48 (10.42%)	
occurrences (all)	4	5	
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
RHINITIS ALLERGIC			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
RHINORRHOEA			

subjects affected / exposed	3 / 8 (37.50%)	6 / 48 (12.50%)	
occurrences (all)	3	6	
SPUTUM DISCOLOURED			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
DEPRESSED MOOD			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
DEPRESSION			
subjects affected / exposed	1 / 8 (12.50%)	3 / 48 (6.25%)	
occurrences (all)	1	3	
INSOMNIA			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
AMYLASE INCREASED			
subjects affected / exposed	1 / 8 (12.50%)	3 / 48 (6.25%)	
occurrences (all)	1	4	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 8 (12.50%)	4 / 48 (8.33%)	
occurrences (all)	1	4	
BILIRUBIN CONJUGATED INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	2	
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	3	3	

BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	1 / 8 (12.50%)	2 / 48 (4.17%)	
occurrences (all)	1	3	
BLOOD CHOLESTEROL INCREASED			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
BLOOD CREATINE INCREASED			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 8 (12.50%)	4 / 48 (8.33%)	
occurrences (all)	1	5	
ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	1 / 8 (12.50%)	2 / 48 (4.17%)	
occurrences (all)	1	2	
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
LIPASE INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
TROPONIN I INCREASED			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
TROPONIN INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
WEIGHT DECREASED			
subjects affected / exposed	3 / 8 (37.50%)	23 / 48 (47.92%)	
occurrences (all)	3	26	
Injury, poisoning and procedural complications			

INFUSION RELATED REACTION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
SCRATCH			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
STOMA SITE HAEMORRHAGE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
ATRIOVENTRICULAR BLOCK FIRST DEGREE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
SINUS TACHYCARDIA			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
TACHYCARDIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	2	
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
DYSGEUSIA			
subjects affected / exposed	0 / 8 (0.00%)	4 / 48 (8.33%)	
occurrences (all)	0	4	
HEADACHE			

subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	3	
LETHARGY			
subjects affected / exposed	1 / 8 (12.50%)	2 / 48 (4.17%)	
occurrences (all)	1	2	
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
POLYNEUROPATHY			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
SOMNOLENCE			
subjects affected / exposed	1 / 8 (12.50%)	2 / 48 (4.17%)	
occurrences (all)	1	2	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	2 / 8 (25.00%)	8 / 48 (16.67%)	
occurrences (all)	3	10	
LEUKOCYTOSIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
NEUTROPENIA			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
PANCYTOPENIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
Eye disorders			
DRY EYE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
EYE DISCHARGE			

subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
VISION BLURRED			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
ABDOMINAL PAIN			
subjects affected / exposed	1 / 8 (12.50%)	3 / 48 (6.25%)	
occurrences (all)	1	5	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 8 (12.50%)	3 / 48 (6.25%)	
occurrences (all)	1	3	
ASCITES			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
CHEILITIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	2	
CONSTIPATION			
subjects affected / exposed	1 / 8 (12.50%)	6 / 48 (12.50%)	
occurrences (all)	1	12	
DIARRHOEA			
subjects affected / exposed	8 / 8 (100.00%)	42 / 48 (87.50%)	
occurrences (all)	12	84	
DRY MOUTH			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
DYSPEPSIA			
subjects affected / exposed	1 / 8 (12.50%)	2 / 48 (4.17%)	
occurrences (all)	1	2	
DYSPHAGIA			
subjects affected / exposed	3 / 8 (37.50%)	4 / 48 (8.33%)	
occurrences (all)	3	4	

GASTRITIS EROSIVE				
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)		
occurrences (all)	0	1		
GASTROOESOPHAGEAL REFLUX DISEASE				
subjects affected / exposed	2 / 8 (25.00%)	3 / 48 (6.25%)		
occurrences (all)	2	3		
GINGIVAL PAIN				
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)		
occurrences (all)	0	1		
GLOSSODYNIA				
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)		
occurrences (all)	0	1		
HAEMORRHOIDS				
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)		
occurrences (all)	0	2		
LIP PAIN				
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)		
occurrences (all)	0	1		
MEGACOLON				
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)		
occurrences (all)	0	1		
NAUSEA				
subjects affected / exposed	4 / 8 (50.00%)	14 / 48 (29.17%)		
occurrences (all)	5	16		
OESOPHAGEAL ACHALASIA				
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)		
occurrences (all)	1	1		
OESOPHAGEAL PAIN				
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)		
occurrences (all)	2	2		
PROCTALGIA				
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)		
occurrences (all)	0	1		
SMALL INTESTINAL OBSTRUCTION				

subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
STOMATITIS			
subjects affected / exposed	3 / 8 (37.50%)	20 / 48 (41.67%)	
occurrences (all)	3	20	
TOOTHACHE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
VOMITING			
subjects affected / exposed	2 / 8 (25.00%)	13 / 48 (27.08%)	
occurrences (all)	2	15	
Hepatobiliary disorders			
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
DECUBITUS ULCER			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
DERMATITIS ACNEIFORM			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	3	
DRY SKIN			
subjects affected / exposed	2 / 8 (25.00%)	6 / 48 (12.50%)	
occurrences (all)	2	6	
ECCHYMOSIS			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
ECZEMA			
subjects affected / exposed	2 / 8 (25.00%)	2 / 48 (4.17%)	
occurrences (all)	2	2	
ERYTHEMA			

subjects affected / exposed	2 / 8 (25.00%)	2 / 48 (4.17%)	
occurrences (all)	2	2	
NAIL TOXICITY			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
PETECHIAE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	2	
PRURIGO			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
PRURITUS			
subjects affected / exposed	0 / 8 (0.00%)	3 / 48 (6.25%)	
occurrences (all)	0	5	
RASH			
subjects affected / exposed	1 / 8 (12.50%)	5 / 48 (10.42%)	
occurrences (all)	1	5	
RASH ERYTHEMATOUS			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
RASH MACULAR			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
RASH PAPULAR			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
SKIN HYPOPIGMENTATION			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
SKIN LESION			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
SKIN REACTION			

subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
SKIN ULCER			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
Renal and urinary disorders			
CHRONIC KIDNEY DISEASE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
HAEMATURIA			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
POLLAKIURIA			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
URETHRAL PAIN			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
URINARY TRACT PAIN			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
Endocrine disorders			
HYPOTHYROIDISM			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	0 / 8 (0.00%)	3 / 48 (6.25%)	
occurrences (all)	0	3	
FLANK PAIN			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
JOINT SWELLING			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
MUSCLE SPASMS			

subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 8 (0.00%)	3 / 48 (6.25%)	
occurrences (all)	0	3	
MYOFASCIAL PAIN SYNDROME			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
NECK PAIN			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
Infections and infestations			
ANGULAR CHEILITIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
BACTERAEMIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
BRONCHITIS			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
CELLULITIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
CLOSTRIDIUM DIFFICILE COLITIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
HERPES ZOSTER			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
LICE INFESTATION			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	

LIVER ABSCESS				
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)		
occurrences (all)	0	1		
LOWER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)		
occurrences (all)	0	1		
LUNG INFECTION				
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)		
occurrences (all)	1	1		
NASOPHARYNGITIS				
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)		
occurrences (all)	0	1		
ONYCHOMYCOSIS				
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)		
occurrences (all)	0	1		
ORAL CANDIDIASIS				
subjects affected / exposed	2 / 8 (25.00%)	4 / 48 (8.33%)		
occurrences (all)	2	4		
OSTEOMYELITIS				
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)		
occurrences (all)	0	1		
PARONYCHIA				
subjects affected / exposed	1 / 8 (12.50%)	2 / 48 (4.17%)		
occurrences (all)	1	2		
RASH PUSTULAR				
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)		
occurrences (all)	0	1		
SINUSITIS				
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)		
occurrences (all)	0	1		
UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)		
occurrences (all)	0	1		
URETHRITIS				

subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	3	
VULVOVAGINAL CANDIDIASIS			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	6 / 8 (75.00%)	31 / 48 (64.58%)	
occurrences (all)	6	34	
DEHYDRATION			
subjects affected / exposed	1 / 8 (12.50%)	5 / 48 (10.42%)	
occurrences (all)	2	7	
HYPERCALCAEMIA			
subjects affected / exposed	2 / 8 (25.00%)	4 / 48 (8.33%)	
occurrences (all)	2	4	
HYPERGLYCAEMIA			
subjects affected / exposed	4 / 8 (50.00%)	23 / 48 (47.92%)	
occurrences (all)	9	48	
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	1 / 8 (12.50%)	1 / 48 (2.08%)	
occurrences (all)	1	1	
HYPERURICAEMIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	
HYPOALBUMINAEMIA			
subjects affected / exposed	2 / 8 (25.00%)	5 / 48 (10.42%)	
occurrences (all)	2	5	
HYPOCALCAEMIA			
subjects affected / exposed	1 / 8 (12.50%)	4 / 48 (8.33%)	
occurrences (all)	1	9	
HYPOKALAEMIA			
subjects affected / exposed	2 / 8 (25.00%)	8 / 48 (16.67%)	
occurrences (all)	5	17	

HYPOMAGNESAEMIA			
subjects affected / exposed	2 / 8 (25.00%)	7 / 48 (14.58%)	
occurrences (all)	3	11	
HYPONATRAEMIA			
subjects affected / exposed	1 / 8 (12.50%)	2 / 48 (4.17%)	
occurrences (all)	3	4	
HYPOPHAGIA			
subjects affected / exposed	0 / 8 (0.00%)	2 / 48 (4.17%)	
occurrences (all)	0	2	
HYPOPHOSPHATAEMIA			
subjects affected / exposed	4 / 8 (50.00%)	8 / 48 (16.67%)	
occurrences (all)	6	14	
METABOLIC ACIDOSIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 48 (2.08%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 May 2013	This amendment clarified that LJM716 and alpelisib will not be dose escalated beyond the MTD determined in the monotherapy Phase I studies.
27 January 2014	The purpose of this amendment was to include ophthalmologic assessments (at the request of a health authority).
17 December 2014	The purpose of this amendment was to include guidelines for management of pneumonitis.

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.

The phase 2 part was not conducted as the study was terminated early due to limited anti-tumor activity with LJM716-alpelisib combination observed in phase 1b.

Notes: